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(71) Applicant: INTERNATIONAL FLAVORS & FRAGRANCES INC.
521 West 57th Street
New York New York 10019(US)

(71) Applicant: YALE UNIVERSITY
451 College Street
New Haven Connecticut 06510(US)

(72) Inventor: Warren, Craig B.
3 Dogwood Lane
Rumson New Jersey(US)

(72) Inventor: Leight, Ronald S.
10 Carol Lane
Aberdeen New Jersey(US)

(72) Inventor: Withycombe, Donald Arthur
10 Roger Avenue
Lincroft New Jersey(US)

(72) Inventor: Mookherjee, Braja Dulal
46 Chestnut Road
Holmdel New Jersey(US)

(72) Inventor: Trenkle, Robert Walter
130 Laurelwood Road
Bricktown New Jersey(US)

(72) Inventor: Munteanu, Marina Alice
301 East 64th Street
New York New York(US)

(72) Inventor: Benaim, Carlos
Windsor Mansion
Hartsdale New York(US)

(72) Inventor: Walter, Henry G. Jr.
Oyster Bay Road
Mill Neck New York(US)

(72) Inventor: Schwartz, Gary E.
326, Colonial Road
Guilford Connecticut(US)

(74) Representative: Baillie, Iain Cameron et al,
c/o Ladas & Parry Isartorplatz 5
D-8000 München 2(DE)

(54) **Methods, compositions and uses thereof for reduction of stress.**

(57) Described is a method for reducing physiological and/or subjective reactivity to stress in humans being subjected to stress conditions. The method consists of administering to such humans an effective amount of a physiological and/or subjective stress reactivity-reducing substance selected from the group consisting of:

(i) Nutmeg Oil;
(ii) Mace Extract;
(iii) Neroli Oil;
(iv) Valerian Oil;
(v) Myristicin;
(vi) Isoelemicin; and
(vii) Elemicin.

Administration is through inhalation or transdermally using one or more of the above ingredients alone or in a suitable composition such as ethanol and/or a perfume composition, cologne or perfumed article (e.g., air freshener or deodorant stick). Also described is a method for detecting the reduction of physiological and/or subjective reactivity to stress in a human.

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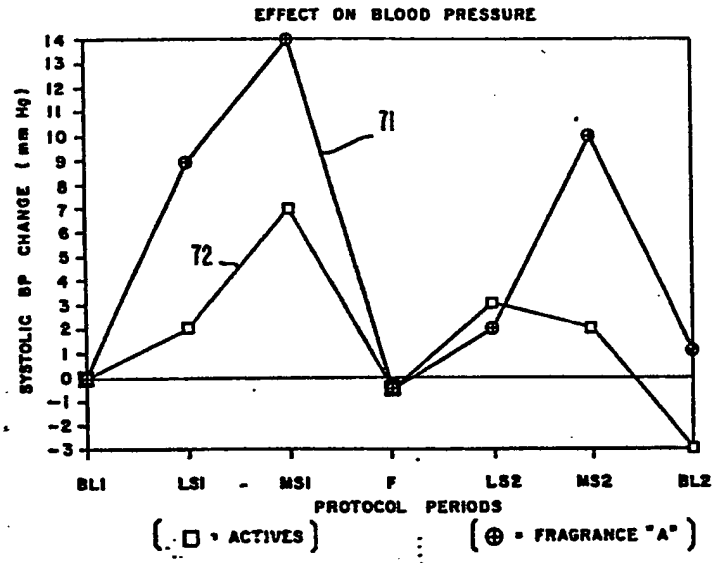
FIG.3
EXAMPLE III



METHODS, COMPOSITIONS AND USES THEREOF FOR REDUCTION OF STRESS

Our invention is concerned with methods and compositions and uses of such compositions for causing the reduction of physiological and/or subjective reactivity to stress in a human subject to stress conditions which comprises the step of administering transdermally or through inhalation to said human an effective physiological and/or subjective stress reactivity-reducing substance which may be one or a combination of any one of the following materials (sometimes referred to herein as "active(s)"):

(i) Nutmeg oil;

(ii) Mace extract;

(iii) Neroli oil;

(iv) Valerian oil;

(v) Myristicin;

(vi) Elemicin; and

(vii) Isoelemicin.

The active(s) can be administered alone or as part of a composition which may include ethyl alcohol and/or perfumes. Perfumed articles may be employed to apply the actives. Examples of such perfumed articles are solid or liquid anionic, cationic, nonionic or zwitterionic detergents, fabric softener compositions, fabric softener articles, cosmetic powders, hair preparations, deodorant sticks, air fresheners and perfumed polymers.

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A preferred mode of this invention is administration through inhalation, and to do so by incorporating the "active(s)" in an enclosed environment such as a room and, accordingly in the atmosphere around the occupant(s) of the enclosed environment. Such is accomplished, for example, by including an "active" in an air freshening composition. Accordingly, another measure for practice of this invention is inclusion of from about 1 up to about 125 micrograms per liter in the air of a room of the stress reactivity-reduction "active(s)" of our invention.

Reduction of physiological and/or subjective reactivity to stress resulting from practice of this invention is demonstrable objectively by means of a decrease in the systolic blood pressure of the human and subjectively in self-report of a significant increase in calmness and happiness and a significant decrease in embarrassment and anger under stress conditions.

The method by which the effect of the stress reactivity reducing substances of our invention has been ascertained is novel. This is the first method that uses a combination of psychological measurements, physiological measurements and a stressor to measure the effect of postulated stress reactivity-reducing substances taken alone or taken further together with ethyl alcohol and/or perfume compositions or perfumed articles or colognes on physiological and/or subjective reactivity to stress.

This invention relates to a process for reducing physiological and/or subjective reactivity to stress in humans subjected to stress conditions. The process involves administering to said humans an effective amount of a stress reactivity-reducing substance hereinafter described.

The term "stress" refers to an event or experience in the life of an individual that has specific physiologic and/or subjective cons quences that disturb the equilibrium of the individual (Glock, C.Y. & Leonard, H.L., Journal

of Chronic Diseases, 1956, 5, 179). Sources of stress may be an individual's occupation, for xampl , controlling air traffic at a busy airport, or it may be a life event change such as a change of job, a death in the family or a divorce, or it may be the small irritations and strains of everyday life---the daily hassles.

The term "reactivity" refers to the change generated by stress in the individual's physiologic and/or subjective condition. Within the context of this invention, "reactivity" may be ascertained objectively by measuring change in systolic blood pressure relative to equilibrium blood pressure resulting from the application of stress. The term "physiologic change" has been employed herein to identify this form of reactivity.

Unlike a drug that is ingested orally or injected subcutaneously, the substances used for the practice of our invention are inhaled and/or absorbed by means of transdermal penetration. Hence, for the purpose of practicing our invention, the term "amount administered" hereinafter is intended to mean "amount of stress reactivity-reducing composition calculated to have been breathed in, retained and absorbed into the bloodstream or transdermally absorbed into the bloodstream".

For the purposes of this invention, a statistically significant increase in systolic blood pressure ($p < 0.1$), is generally 3mm/Hg or more due to the stress.

Hereinafter, the subjective reactivity to stress is a statistically significant change ($p < 0.05$) in the individual's self-report of one or more of the following emotions:

Decrease in degree of relaxation;
Decrease in happiness;
Decrease in calmness;
Increase in fear;
Increase in tenseness;
Increas in embarrassm nt;

Increase in anger; and/or

Increase in anxiety.

Reactivity to stress varies with the individual. Some individuals thrive on stress whereas in other individuals, the same stress drives them towards sickness (Executive Fitness Newsletter, Rodale Press Inc., Vol. 15, No. 17 [1984]). "Reactivity" hereinafter refers to a negative reaction to stress.

"Reactivity" to stress should not be confused with the abnormally high base-line blood pressure or anxiety levels which may require drug treatment. For example, it should not be confused with hypertension which is defined as blood pressure that remains consistently above 140mm/Hg systolic and 90mm diastolic pressure with repeated blood pressure determinations over the course of several weeks (Report of the Joint National Committee on Detection, Evaluation and Treatment of High Blood Pressure; Journal of the American Medical Association, 1977, 277, 255-261).

It is appreciated that reactivity and hypertension or state of anxiety may be related. Abnormal anxiety or depression has as its major primary causative components the fundamental conditions of helplessness, uncertainty, anticipation, undirected arousal and the like (Zucker, M. & Spielberger, C.D., "Emotions and Anxiety", Lawrence Erlbaum Associates, Publishers; Hillsdale, New Jersey [1976]). See, also, The Diagnostic and Statistical Manual of the American Psychiatric Association, DSM3, 1980.

Our invention is further defined and as follows:

(i) Modern medicine and much of aromatherapy alike are largely devoted to healing of the sick. The practice of this invention is directed to alleviation of physiological and/or subjective stress-induced reactivity in persons of a level not requiring the attention of the medical practitioners. Usually the r activity to an ordinary stress situation (reactivity being measurabl

by a puls -like elevation in systolic blo d pressure) will not be acc mpani d by any untoward observable reaction.

As a result, although substances employed in practice of this invention are known to have physiologic activity, they are suggested in folk medicine and aromatherapy within a different use context than practice of this invention. For example, Valnet, "The Practice of Aromatherapy", Destiny Books (Division of Inner Traditions International, Ltd.), New York, New York, 1982, advises that nutmeg oil is an analgesic (when applied externally) and advises of internal (but not external) use for neroli oil. R. Tisserand, "The Art of Aromatherapy", Destiny Books (Division of Inner Traditions International, Ltd.), New York, New York, 1983, advises that neroli oil makes a luxurious, relaxing and deodorant bath oil (which is in keeping with his report that neroli oil is one of the most effective sedative anti-depressant oils, and useful for insomnia, hysteria, states of anxiety and depression).

The aromatherapy and folk medicine literature, supra, cite the mode of administration as oral ingestion of gram quantities of material or application of gram quantities massaged over the body. None of the literature known to the inventors hereof suggests that inhalation or transdermal absorption of microgram quantities of the plant-derived substances or their synthetic counterparts (described in this invention) will reduce physiological and/or subjective reactivity to stress.

(ii) The results obtained through practice of this invention are comparable to results obtainable from meditation and biofeedback, including, notably, damping of the systolic blood pressure surges arising from stressful situations. However, unlike meditation or biofeedback, no training period is required in the use of the stress reactivity-reducing substances of our invention. Th effect of the str ss r activity-reducing substances

of our invention occurs within four minutes after inhalation of said substances.

(iii) Unlike anti-anxiety drugs, the effect of the volatile compositions of matter employed in the practice of our invention, (e.g., nutmeg oil, mace extract, neroli oil, valerian oil, myristicin, elemicin and/or isoelemicin) is prophylactic in nature, reducing (the physiological and/or subjective) reactivity to stress when stress conditions exist. Unstressed people do not respond to the method of this invention.

Thus, inclusion of actives in a bath oil composition does not fall within the practice of this invention for reason that bathing normally takes place sometime after occurrence of stressful situations. It is noted, however, that the relaxing effect attributed by Tisserand, supra, to neroli oil-containing bath oils may well be an effect on persons whose reactivity to stress does not subside for many hours.

(iv) Practice of this invention may be distinguished from the prior art employment of active essential oils, e.g., from nutmeg, in perfume compositions. Aside from generating presence of the actives in the surrounding atmosphere at a concentration less than is effective to reduce reactivity to stress, perfume usage in modern day practice involves employment during non-stress occurring situations.

DESCRIPTION OF THE DRAWINGS

Figure 1 is the GLC profile of the head-space above nutmeg oil measured according to the procedure of Example I(B) (Conditions: OV-1 fused silica column programmed at 75-220°C. at 2°C. per minute). The nutmeg oil is East Indian Nutmeg Oil.

Figure 2 is the GLC profile for bulked fraction 7-12 of the second distillation of nutmeg oil East Indian according to the procedure of Example I(A) (Conditions: 400' x 0.032" carbowax/fused silica column programmed at 75-220°C. at 2°C. per minute).

Figur 3 sets forth the effect on blood pressure changes (of a human subject to str ss conditions) of:

(i) a composition of "actives" as set forth in Example II according to the protocol of Example III; and

(ii) a fragrance composition entitled fragrance "A" specifically described according to Example II

with the changes in blood pressure being in units of mm/Hg.

The graph indicated by reference numeral 71 is the graph of systolic blood pressure (mm/Hg) versus protocol period (e.g., BL1, LS1, MS1, F, LS2, MS2 and BL2) defined in Example II for fragrance "A"; that is, the fragrance that does not contain "actives", e.g., nutmeg oil, mace extract, neroli oil and valerian oil. The protocol periods are as follows:

BL1 - baseline in "Stress I";

LS1 - 6 low stress questions in "Stress I";

MS1 - 6 mild stress questions in "Stress I";

F - two blood pressure points during application of fragrance "A" between "Stress I" and "Stress II";

LS2 - 6 low stress questions in "Stress II";

MS2 - 6 mild stress questions in "Stress II";

BL2 - baseline at end of "Stress II".

The graph indicated by reference numeral 72 is the graph of systolic blood pressure (mm/Hg) versus protocol period when using the "actives" mixture, that is, the mixture of nutmeg oil, mace extract, neroli oil and valerian oil "actives composition" of Example II using the protocol of Example III. The meaning of each protocol period is the same as described above except the period "F" during which "Actives" was administered.

Figure 4 sets forth the effect on blood pressure (of a human subject to stress conditions) of a composition of "actives" (as set forth in Example II) according to

the protocol of Example III and in combination with a fragrance composition denoted as fragrance "A", with the blood pressure being in units of mm/Hg and with the measurements being made according to the procedure of Example IV.

The graph indicated by reference numeral 81 is the graph of systolic blood pressure (mm/Hg) vs. protocol period (e.g., BL1, LS1, MS1, F, LS2, MS2 and BL2) defined in Example IV for the combination: fragrance "A" and "actives", e.g., nutmeg oil, mace extract, neroli oil and valerian oil.

Our invention necessarily also involves a method for detecting physiological and/or subjective reactivity to stress in a human comprising testing a human likely to exhibit physiological and/or subjective reactivity by:

(i) measuring the initial blood pressure and mood of said human; then

(ii) administering stress to said human by means of application of a stressor;

(iii) simultaneously measuring blood pressure change and mood change resulting from the application of said stress to said human; thereafter

(iv) administering a postulated stress reactivity-reducing substance to said human; and

(v) simultaneously measuring the blood pressure change and mood change in said human resulting from the application of said postulated stress reactivity-reducing substance during the application of said stressor to said human.

As has already been pointed out, our invention is directed to a method for causing the reduction of physiological and/or subjective reactivity to stress in a human being subjected to stress conditions which comprises administering to said human an effective amount of a substance which may be on or a mixture of:

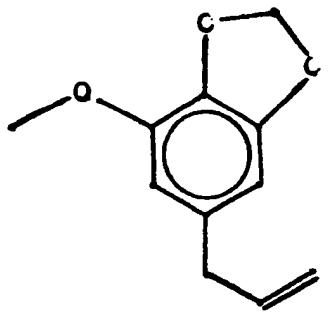
Nutmeg oil;

Mace extract;

Neroli oil;

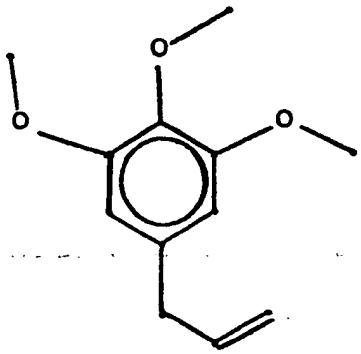
Valerian oil;

Myristicin having the structure:



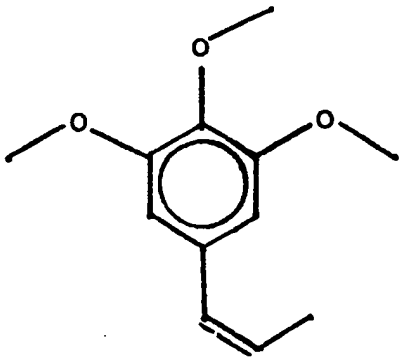
;

Elemicin having the structure:



; and/or

Isoelemicin having the structure:

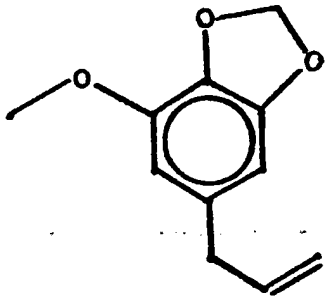


taken alon or taken further togeth r with a carrier which may be a perfumed articl or cologn and/ r ethanol.

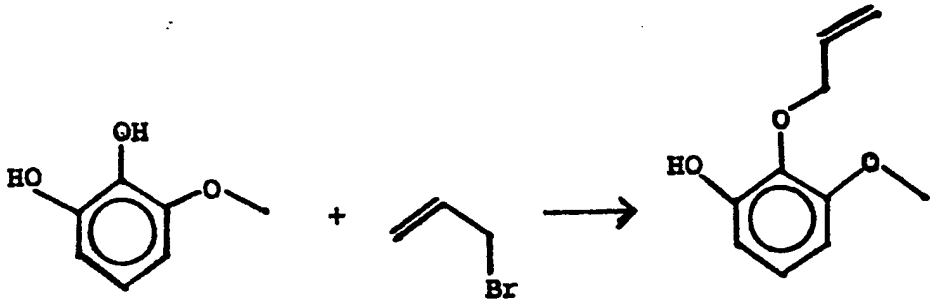
Insofar as th nutmeg oil, mace extract, n roli oil and valerian oil are concerned, the various varieties of such materials are useful in the practice of our invention. Thus, for example, Nutmeg Oil East Indian or Nutmeg Oil West Indian are useful in the practice of our invention. Standard commercial mace extract is useful in our invention as is the more highly purified form thereof. Commercial valerian oil is useful in the practice of our invention as is the refined version, doubly distilled valerian oil.

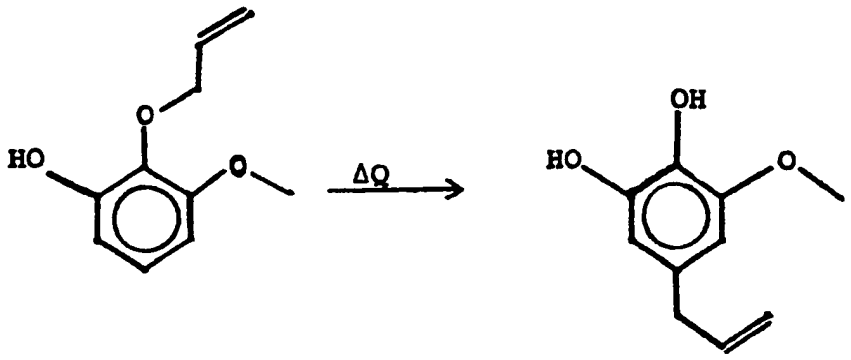
In addition, naturally occurring or synthetically produced myristicin, elemicin and isoelemicin are useful in the practice of our invention.

Thus, myristicin having the structure:

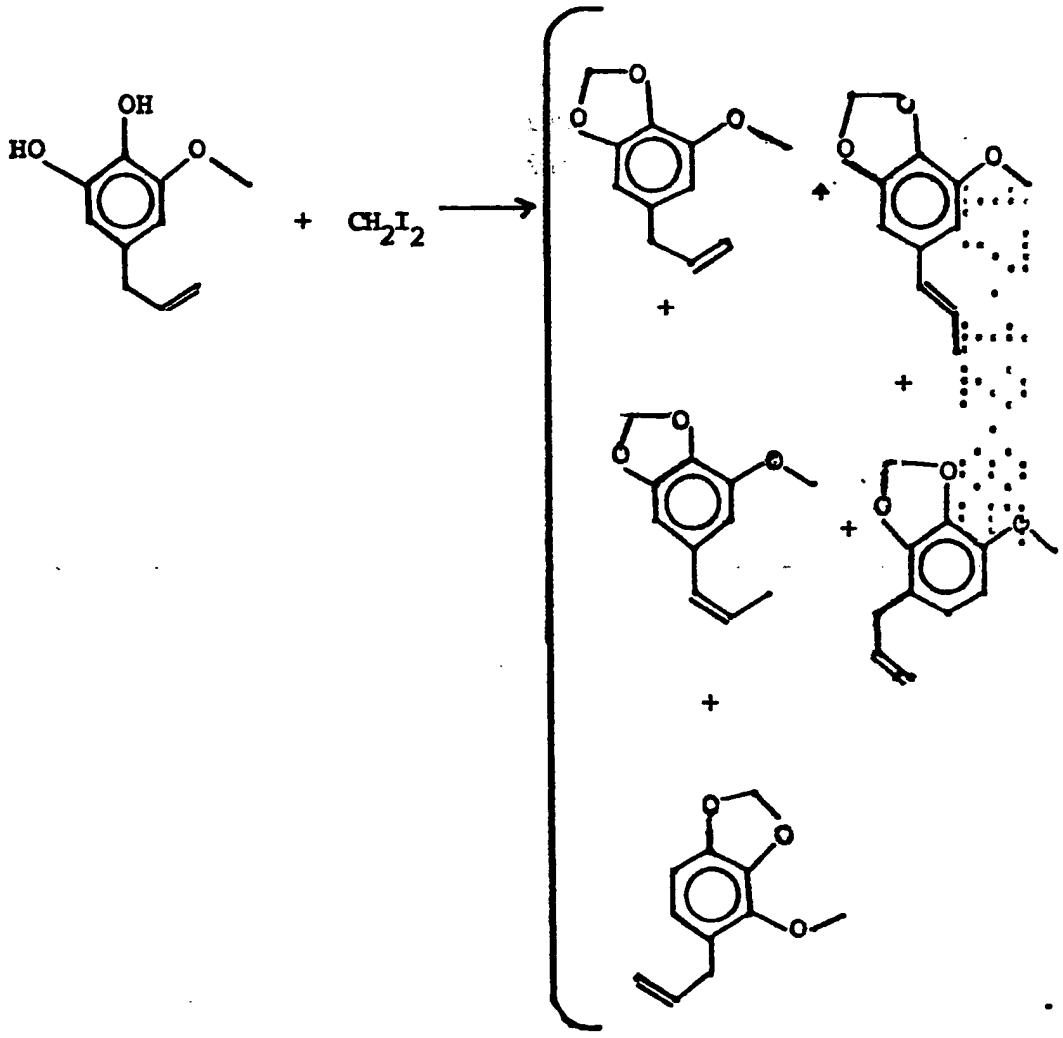


may be isolated as by distillation from Nutmeg Oil East Indian or West Indian or Nutmeg Oil Fiji or it may be synthesized according to the reaction sequence:





; and



Thus, our invention is directed to the use of one or a mixture of the following ingredients:

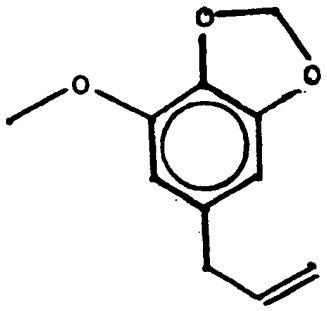
Nutmeg Oil;
Mace Extract;
Valerian Oil;
Neroli Oil;
Myristicin;
Elemicin; and/or
Isoelemicin,

which ingredients, i.e., the "active(s)", may be administered alone or further together with a "non-active" carrier composition (such as (i) ethanol or (ii) a carrier perfume composition or (iii) a carrier perfumed article) for the reduction of physiologic change and/or subjective manifestations of reactivity in a human being subjected to stress conditions. This reduction in reactivity decreases the systolic blood pressure surges caused by stress and generates a significant increase in calmness and happiness and a significant decrease in embarrassment and anger in said human. The physiological change and subjective manifestations of reactivity to stress and a reduction of reactivity to "stress" are quantifiable, see Examples II, III, IV and V, infra.

To repeat, the "active" stress reactivity-reducing substances of our invention, to wit:

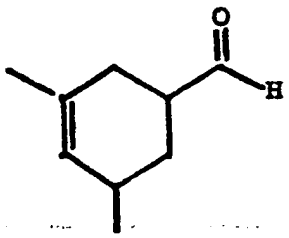
Neroli Oil;
Mace Extract;
Nutmeg Oil;
Valerian Oil;
Myristicin;
Elemicin; and
Isoelemicin

are, in their own right, perfumery substances known in the prior art. For example, myristicin having the structure:

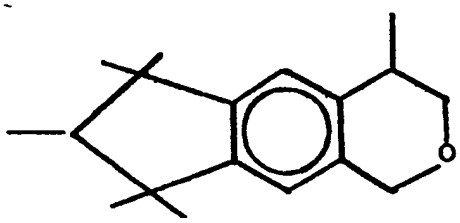


contributes an interesting spicy aroma to perfumes.

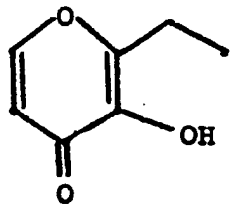
However, the terms "carrier perfume" and "carrier perfume composition" are used herein within an inert carrier context to mean mixtures of organic compounds (other than such "actives") including, for example, fragrant alcohols, fragrant aldehydes such as, for example, the aldehyde having the structure:



ketones, nitriles, ethers such as, for example, the cyclic ether having the structure:



and the cyclic ether having the structure:



(but excluding, of course, elemicin, isoelemicin and myristicin), and such materials as lactones, hydrocarbons, synthetic essential oils and natural essential oils (excluding, of course, the natural essential oils: nutmeg oil, valerian oil, neroli oil and mace extract) in admixture so that the combined odors of the individual components produce a pleasant or desired fragrance.

Although state of the art perfume and cologne compositions are contemplated for carrier purposes in practice of this invention, the "actives" are fragrances, and therefore some comments here about perfumery practices are warranted.

Perfume compositions usually contain (a) the main note or the "bouquet" or foundation stone of the composition; (b) modifiers which round off and accompany the main note; (c) fixatives which include odorous substances which lend a particular note to the perfume throughout all stages of evaporation and substances which retard evaporation; and (d) topnotes which are usually low-boiling fresh smelling materials.

In perfume compositions, each individual component will contribute its particular olfactory characteristics but the overall effect of the perfume composition will be the sum of the effects of each ingredient. Thus, individual perfumery compounds or mixtures thereof can be used to alter the aroma characteristics of a proposed perfume composition, for example, by highlighting or moderating th lfactory reaction contributed by another ingredient in the composition. The "actives" of this invention will alter the aroma

characteristics of a carrier perfum composition in addition to causing str ss r activity reduction in a human who is subjected to stress conditions. Therefore the aroma desired for the composition as a whole, rather than the aroma of the carrier perfume formulation alone, should be made the basis upon which the carrier perfume composition is formulated.

It should be appreciated that a perfume or cologne composition containing "actives" is being administered by inhalation, and, to the extent the composition has been applied to the skin, transdermally as well. Air freshener compositions are administered almost entirely through inhalation.

The amount of the stress reactivity reduction perfume composition required for effective action (with regard to the user) depends on many factors including the skin condition of the user; the environmental conditions during the period of desired effectiveness (e.g., humidity, temperature and pressure), the emotional state of the user at the point in time of application; the physical characteristics of the user including body weight and base line systolic blood pressure at the point(s) in time of application(s). All of which is to say that individual reactivity and feelings of comfort by a user will determine the amount effective for that user.

The perfume composition may be used "as is" (e.g., 100%) or in a "cologne". Directions for quantity to use and frequency of use, as well as variations in the formulation, e.g., summer and winter formulations, may be employed to assure that effective levels of the "actives" may be administered. For the purpose of this invention, the term "cologne", as exemplified hereinafter, means a perfume composition incorporated in an alcoholic or hydroalcoholic solution. The perfume composition can vary between 1 to 99% and the balance of the formulation is compris d of alcohol or a mixture of water and

alcohol. Th wat r:alcohol weight ratio can vary from 50:50 to 0:100. Examples of alcohols typically used in these products are SDA 39-C and SDA-40, either 190 "proof" or anhydrous (See "Ethyl Alcohol Handbook", 5th Edition, Published by National Distillers and Chemical Co.). The cologne composition can also contain solubilizing agents, emollients, humectants, thickening agents, bacteriostats or other cosmetically-used ingredients.

Although perfume compositions and colognes would normally be considered to administer the "actives" by inhalation or smelling, placement thereof on the epidermal skin tissue generates, also, transdermal penetrative administration.

Perfumery materials which are compatible with the stress reactivity reduction substances have been employed in aromatizing carrier perfumed articles. Such perfumed articles include fabric softener compositions, dryer-added fabric softener articles, e.g., BOUNCE® (a Registered Trademark of the Procter & Gamble Company of Cincinnati, Ohio), cosmetic powders, talcs, solid or liquid anionic, cationic, nonionic or zwitterionic detergents and perfumed polymers as well as deodorant sticks, hair preparations and bar soaps as exemplified, infra.

Furthermore, perfume materials which are compatible with the stress reactivity-reducing substances of our invention have been employed in air fresheners. Thus, a great number of state-of-the-art perfume compositions and perfumed articles are available for use as the non-active carrier (perfumed) composition and (perfumed) articles within which the "actives" may be incorporated for practice of this invention.

Thus, the stress reactivity-reducing substances can be used along or taken together with carrier perfume compositions alone or through carrier perfumed articles. When perfume compositions are used as an olfactory

component of a perfumed articl , such as a solid or liquid anionic, cationic, nonionic or zwitt rionic detergent or a cosmetic powd r or a deodorant stick, as little as 0.1% by weight of the overall perfume and stress reactivity-reducing "active(s)" (in combination) in the perfumed article will suffice. In space odorant applications, on the other hand, as much as 99% of the combined carrier perfume substance and stress reactivity-reducing substance can be present. Thus, perfumed articles may contain in the range of from about 0.1% up to about 99% of a composition of matter consisting essentially of the stress reactivity-reducing "active(s)" and "non-active" carrier perfume substance.

It is interesting to note that when a stress reactivity-reducing "active" is used in a deodorant stick or deodorant bar soaps to practice our invention, a twofold effect takes place;

(i) the deodorant stick itself acts as a "deodorant" in the auxillary area of the human being; and

(ii) the stress reactivity-reducing "active(s)" is administered by inhalation or transdermally to cause reduction in physiological and/or subjective reactivity to stress in those individuals subjected to stress conditions.

The term "perfumed article" also includes solid-form polymers, such as polyethlene, polypropylene and other polymers which contain pores within which are occluded a carrier perfume composition combined with the stress reactivity-reducing "active(s)". Such perfumed polymers can be produced as described herein or according to any technique well known to one having ordinary skill in the art.

The active compounds described herein may also be administered in the form of a toothpaste composition.

In addition, the stress reactivity-r ducing

substances of our invention, .g., neroli oil, nutm g oil, mac extract, valerian oil, myristicin, elemicin and isoelemicin taken alon or taken in combination may, by themselves, be absorbed into the interstices of microporous or macroporous polymers. Furthermore, like carriers of materials other than synthetic polymers can be used to generate a "perfume article" such as a gum (e.g., guar gum, xanthan gum, or gum arabic) or an encapsulating composition such as a gelatin (as by coacervation) or such as a urea/formaldehyde prepolymer to form a urea/formaldehyde polymeric wall around a liquid center, which liquid center contains the stress reactivity-reducing "active(s)" alone in conjunction with ethanol and/or a carrier perfume composition.

Unlike anti-anxiety drugs, as mentioned supra, the effect of the "actives" materials is to reduce the physiological and/or subjects reactivity to stress in a person who is subjected to stress conditions. Individuals who are not being subjected to stress conditions do not react to the administration of any of the above-mentioned "active(s)" according to the practice of this invention.

Unlike meditation or biofeedback, no training period is required for the human who is to be treated in order to effect reduction of physiological and/or subjective reactivity to stress. The effect(s) of an "active" material, e.g., nutmeg oil, mace extract, neroli oil, valerian oil, myristicin, elemicin and isoelemicin, occurs within four minutes after initial inhalation or smelling of the substance by the individual under stress to whom the substance is administered.

The weight ratio of stress reactivity-reducing "active(s)" to the ingredients in the carrier perfume composition, cologne or the perfumant applied to generate the carrier perfumed article is in the range of from about 1:100 up to about 100:1. It is emphasized that the carri r perfume composition, cologne and perfumant applied to g nerate the carri r perfumed articl do not

otherwise contain any other stress-reactivity reducing substanc s, or for that matt r any stress-affecting or hypotensive substances employed in the medical arts, for example, benzodiazepine derivatives for anxiety and methyldopa or propranolol for hypertension.

Our invention expressly contemplates the use of ethyl alcohol in conjunction with the "actives". The ethyl alcohol may enhance the efficacy of the "actives". As has already been pointed out ethyl alcohol is a major component in standard cologne compositions.

When the stress reactivity-reducing "active(s)" is used in conjunction with ethyl alcohol, the weight ratio of "active(s)" to the ethyl alcohol (based upon pure ethanol) is in the range of from about 1:99 up to about 99:1. The ethanol used in conjunction with practice of our invention may vary from 50% aqueous ethanol up to 100% (absolute ethanol).

One great advantage of the practice of this invention for the reduction of physiological and/or subjective reactivity to stress in humans is the fact that the dose level of "active(s)" is miniscule; being of the order of micrograms.

Specifically with regard to dose levels, the "actives" are to be divided into two groups:

Group "ALEPH"

Nutmeg oil;
Mace extract;
Neroli oil; and
Valerian oil
(taken alone or in combination)

Group "BETH"

Myristicin;
Elemicin; and
Isoelemicin
(taken alone or in combination).

The group "ALEPH" d se for th purpose of our invention is from about 13 micrograms up to about 1000

micrograms. Th group "BETH" dose for th purpose of our invention is from about 0.013 micrograms up to about 50 micrograms.

When materials from the Groups "ALEPH" and "BETH" are used in combination, the dosage of "actives" is from about 0.013 micrograms up to about 1000 micrograms with an upper limit of the Group "BETH" component within said combination being about 50 micrograms.

The term "amount" administered" is intended herein to mean "amount calculated to have been breathed in, retained and absorbed into the bloodstream or transdermally absorbed into the bloodstream". The assumptions that underlie the calculations of the above levels are presented in Tables I and II and associated text, infra.

Reverting to "active(s)" dosage ranges in general, at the upper bound of the ratio of weight of a carrier perfumed composition (containing no "actives"): weight of "active" Group "ALEPH" (that is, 100:1), the total amount of perfume composition used requires a range of from about 13 micrograms up to about 1000 micrograms "active" and thus requires a range of from about 1300 micrograms (1.3 mg) up to about 100,000 micrograms (0.1 gm) of non-active-containing carrier perfume composition. Furthermore, at the upper bound of the ratio of weight of perfume composition (containing no "actives"):weight of "active" Group "BETH" (that is, 100:1), the total amount of perfume composition used contains a range of from about 0.013 micrograms up to about 50 micrograms "actives" and thus constitutes a range of from about 1.3 micrograms up to about 5000 micrograms (5 mg) of non-active-containing carrier perfume composition.

By the same token, at the lower limit of the ratio of weight of a carrier perfume composition (containing no "activ s"):weight of "active" Group "ALEPH" (that is, 1:100), the total amount of perfume composition requir s a range of from about 13 micrograms up to about

1000 micrograms "actives" and thus requires a range of from about 0.13 micrograms up to about 10 micrograms of non-active-containing perfume composition. At the said lower limit, the ratio of weight of p rfume composition (containing no "actives"):weight of "active" Group "BETH" (that is, 1:100), the total amount of perfume composition used nonetheless contains a range of from about 0.013 micrograms up to about 50 micrograms "actives" and thus constitutes a range of from about 0.00013 micrograms up to about 0.50 micrograms of non-active carrier perfume composition. Thus, the working ranges of perfume + "active") compositions contemplated within the scope of the invention vary as follows:

(a) For Group "ALEPH" "actives" - from 13 micrograms up to 100,000 micrograms (0.1 grams); and

(b) For Group "BETH" "actives" - from 0.013 micrograms up to 5000 micrograms (5 mg).

As previously stated, perfumed articles contemplated within the scope of this invention may contain in the range of from 0.1% up to 99% by weight of combined non-active carrier perfume and "active(s)". The range of 0.1-99.0 gms of perfume composition per 100 grams of article should be considered guidelines rather than strict limits.

It therefore follows that 100 grams of a perfumed article employed in practice of our invention will contain from about 0.1 grams up to about 99.0 grams of a perfume composition that includes "active(s)".

It follows also that practical restraints exist upon practice of this invention through perfumed articles. For example, when administration of "actives" from perfumed garments is desired, transfer of "actives" to the garments from perfumed detergent may not be practical. However, transfer from a perfumed fabric softener to the fabric is more feasible. More often than not practical restraints simply challenge the skill of the formulator when administration is sought from per-

fumed deodorant compositions, cosmetic powders, hand soaps, and th like, for example. Some perfumed articles offer less of a challeng to the formulator, or no challenge at all; air freshener compositions, for example.

Some uncertainty is acknowledged also for the administration range of 13-1000 micrograms of "ALEPH" group "active(s)" and 0.013-50, 13-1000 micrograms of "ALEPH" group "active(s)" and 0.013-50 micrograms of "BETH" group "active(s)". The experimental effort underlying this invention may not translate exactly to the dosage range suited to large scale practice of this invention, for (necessarily) having been conducted under artificial conditions. For better understanding of this invention, and as aid to translation of the exemplary material herein into large scale practice of the invention, details of the experimental conditions and dosage assumptions made by the inventor hereof are now provided.

In specific, the effective dose levels for Groups "ALEPH" and "BETH" set forth above constitute estimates of quantities breathed in and effectively taken up by the subjects from a perfumer's blotter as described in Example II, infra, or from a wick-vial arrangement as described in Example III and IV, infra.

The source of the stress reactivity reduction composition was about 1.5 inches from the subject's nose. For the estimation of dosages, the following assumptions were used:

1. Breathing rate for an average subject at rest is 10 liters per minute.
2. The total amount of substance breathed in and

retained is 25% of the material that is evaporating. We assumed intake of 50% of the material evaporating from the source. Of the material breathed in, 50% was subsequently exhaled.

3. The total amount of the substance effectively taken up by the body is about 10% of the breathed in and retained substance.
4. The average body weight of a human being is 65 kg.

The assumptions used for estimation of dosages were based on measured plasma levels for Δ^9-tetrahydrocannabinol (Δ^9THC) that had been administered by inhalation of marihuana smoke. For this situation 50% of the Δ^9-THC breathed in was retained and approximately 10% of the retained material was found in the plasma. (Nahas, G. and Paton, D., eds., "Marihuana: Biological Effects", in Advances in the Biosciences, Vols. 22/23, Pergamon Press, N.Y., [1979], page 289). In addition to the above assumptions, the following parameters were measured:

1. The amount of substance evaporating from the source of postulated stress reactivity-reduction composition was obtained by weight loss measurements.
2. The concentration of Group "BETH" component(s) e.g., Myristicin, Elemicin and Isoelemicin in the head-space was measured by gas chromatography.
3. The total time that the subject breathed the stress reactivity-reduction substances was 20 minutes.

The following Tables I and II present a summary of our results.

TABLE I - Evaporation Rates for Stress Reactivity Substances and Non-Active-Perfume Containing Substance

Example	Evaporation Rate (mg/min)		% Actives	Calculated Evaporation Rate Group "ALEPH" Component (mg/min) (a)	Amount of Group "BETH" Component in Group "ALEPH" Component Being Evaluated (micrograms/min) (b)
	Oil Containing Actives and Non-Active-Containing-Perfume Composition	Ethyl Alcohol			
II	0.12	0.18	40	0.05	0.05
III	0.26	0.26	100	0.26	0.26
IV	0.15	-	40	0.06	0.06
Fragrance B	0.26	0.26	2	0.005	0.005

Notes: a) The calculated evaporation rate of the Group "ALEPH" component is the evaporation rate of the oil-containing "actives" x the percent "actives" in the oil.

b) The amount of Group "BETH" component in Group "ALEPH" was determined by gas chromotography (see Example I) to be approximately 0.1% of the "ALEPH" concentrations.

TABLE II - Concentrations Breathed in and Retained and Concentrations Absorbed

Example	Amount Breathed in and Retained (micrograms/min)	Assumed Amount Group "ALEPH" Component absorbed into Bloodstream (micrograms/min)	Amount Group "BETH" Component (Part of Group "ALEPH" Component Absorbed (micrograms/min)
II	13	1.3	0.0013
III	65	6.5	0.0065
IV	15	1.5	0.0015
Fragrance B	1.3	0.13	0.00013

Suggested Levels Compositions

1. Concentrations in Air Space:

Assume amount breathed in/breathing rate. [This is equal to the vaporation rate for "ALEPH" or "BETH" divided by two to correct for the amount not breathed in, divided by the breathing rate which is assumed to be 10 liters per minute].

TABLE III

	Apparent Amount in Air Space of Stress Reactivity Reduction Substance (Micrograms per liter)	
Example	Group "ALEPH" Component	Group "BETH" Component Contained in Group "ALEPH" Component
II	2.50	0.00250
III	13.00	0.01300
IV	3.00	0.00300
Fragrance B*	0.25	0.00025

2. Dose Levels. Minimum Dose Level is Amount Effectively Absorbed for Example II x 10 min.

Minimum = 13 micrograms of Group "ALEPH" Component and 0.013 micrograms of Group "BETH" component

Maximum dose level is estimated from folk medicine literature suggestions for soothing bath oil and other external uses for the actives. Parenthetically, it is noted that the maximum dose level is estimated to be about 1% or less of the quantities reported to have stupefacient activity.

* Fragrance B is a prior art perfume composition containing nutmeg oil. This fragance was evaluated for reasion that it contains the highest level of any actives in the perfumes known to the inventors hereof. The quantity of actives administered is about 10% of the minimum dose level for practice of this invention.

Although the experimental data is limited to administration through inhalation which treatment mode involves transport of "actives" across internal body membranes, the "active(s)" are known to transport across external body membranes, notably across epidermal tissue (see, for example, disclosures of external application of "actives" in folk medicine and aromatherapy arts). Practice of this invention includes, then, both transdermal administration, and through inhalation with, it is believed, the same dosage range for treatment by either treatment mode.

The following Examples II, III, IV and V set forth processes for preparing and testing stress reactivity-reducing compositions of our invention. Examples following Example V, e.g., Example VI, et seq, set forth incorporation of the stress reactivity-reducing substances in perfumed articles.

The following Example I sets forth methods for analyzing and producing certain of the stress reactivity-reducing substances, e.g., myristicin and elemicin and the like.

It is to be understood that the invention is not to be so limited to the embodiments herein exemplified.

EXAMPLE I(A)

ISOLATION OF MYRISTICIN FROM EAST INDIAN NUTMEG OIL AND HEAD SPACE ANALYSIS OF EAST INDIAN NUTMEG OIL

East Indian Nutmeg Oil was carefully distilled on a 1 plate short path column yielding the following fractions:

FRACTION NO.	VAPOR TEMP. (°C.)	LIQUID TEMP. (°C.)	VACUUM psia	WEIGHT of FRACTION (gms)
1	43/42	47/46	20/20	26.2
2	42	47	20.0	77.6
3	43	48	20.0	73.1
4	45	52	20.0	67.0
5	45	52	20.0	84.0
6	45	54	20.0	67.6
7	47	63	20.0	58.4
8	49	76	20.0	62.5
9	63	82	5.0	38.4
10	71	100	1.2	45.0
11	94	108	1.2	14.3
12	98	111	1.2	24.6
13	100	117	1.2	26.9
14	96	130	1.1	17.9
15	100	180	1.0	10.5

Fractions 13 and 14 were bulked and further purified by means of distillation on a spinning band distillation column (Nester Faust Auto Annular Distillation Unit) yielding the following fractions:

FRACTION No.	VAPOR TEMP. (°C.)	LIQUID TEMP. (°C.)	VACUUM mm/Hg PRESSURE	WEIGHT of FRACTION (gms)
1	68/72	156/158	0.6/0.6	1.7
2	72	161	0.60	2.9
3	74	161	0.60	3.6
4	72	158	0.60	4.2
5	70	156	0.60	3.5
6	74	157	0.65	3.2
7	71	159	0.50	4.2
8	71	160	0.55	4.9
9	71	159	0.55	3.6
10	71	161	0.55	2.5
11	71	169	0.55	2.5
12	66	185	0.55	1.7

Fractions 7-12 are bulked.

Figure 1 is the GLC profile for bulked fractions 7-12 of the foregoing distillation (conditions: 400 x 0.032" fused silica/carbowax column programmed at 75-220°C. at 2°C. per minute).

The thus-produced substantially pure myristicin was used for further experiments as set forth in Example II, et seq.

EXAMPLE I(B)

HEAD SPACE ANALYSIS OF NUTMEG OIL AND MACE OIL

2 Grams of Nutmeg Oil East Indian or Mace Oil was placed in a 250 cc single neck receiver. The receiver was fitted with a rubber stopper into which was embedded a stainless steel hook. On the hook was placed a 2 cm^2 stainless steel screen impregnated with dioctylphthalate. The dioctylphthalate absorbed the ingredients of the head space above the nutmeg oil for a period of 15 minutes. At the end of the 15 minute period, the stopper with the screen was removed from the flask and the screen was removed from the hook. Th

screen was then placed in a small clinical c nterfuge and the dioctylphthalate containing the ingredients of the head space was separated from the screen by m ans of centrifugation. The resulting product was then subjected to GLC analysis (Conditions: OV-1 fused silica column programmed at 75-220°C. at 2°C. per minute).

Figure 2 is the GLC profile for the head space above the nutmeg oil.

The peak indicated by reference numeral 10 is the peak for α-thujene.

The peak indicated by reference numeral 11 is the peak for α-pinene.

The peak indicated by reference numeral 12 is the peak for sabinene.

The peak indicated by reference numeral 13 is the peak for β-pinene.

The peak indicated by reference numeral 14 is the peak for myrcene.

The peak indicated by reference numeral 15 is the peak for α-phellandrene.

The peak indicated by reference numeral 16 is the peak for δ-3-carene.

The peak indicated by reference numeral 17 is the peak for α-terpinene.

The peak indicated by reference numeral 18 is the peak for p-cymene.

The peak indicated by reference numeral 19 is the peak for γ-terpinene.

The peak indicated by reference numeral 20 is the peak for terpinolene.

The peak indicated by reference numeral 21 is the peak for linalool.

The peak indicated by reference numerals 22A and 22B are the peaks for 1-hydroxy-1-methyl-4-isopropyl-2-cyclohexene.

The peak indicated by ref r nce numeral 23 is the peak for 2-methyl-5-ethyl furan.

The peak indicated by reference numeral 24 is th peak for 4-terpineol.

The peak indicated by reference numeral 25 is the peak for α-terpineol.

The peak indicated by reference numeral 26 is the peak for 1-methyl-3-hydroxy-4-isopropenyl benzene.

The peak indicated by reference numeral 27 is the peak for isobornyl acetate.

The peak indicated by reference numeral 28 is the peak for n-amyl methoxy benzenes.

The peak indicated by reference numeral 29 is the peak for eugenol.

The peak indicated by reference numeral 30 is the peak for α-terpinyl acetate.

The peak indicated by reference numeral 31 is the peak for α-cubebene.

The peak indicated by reference numeral 32 is the peak for eugenyl methyl ether.

The peak indicated by reference numeral 33 is the peak for α-copene.

The peak indicated by reference numeral 34 is the peak for trans-isoeugenol.

The peak indicated by reference numeral 35 is the peak for α-bergamotene.

The peak indicated by reference numeral 36 is the peak for 4-propenyl-1,2-dimethoxy benzene.

The peak indicated by reference numeral 37 is the peak for myristicin.

The peak indicated by reference numeral 38 is the peak for δ-cadinene.

The peak indicated by reference numeral 39 is the peak for elemicine.

The peak indicated by reference numeral 40 is the peak for 4-allyl-2,6-dimethoxyphenol.

Table IV sets forth the head space constituents of nutmeg oil after the 15 minut s period using the proc dur set forth, supra; after a on hour p riod, using the procedure set forth, supra, and after a 24 hour period, using

the procedure set forth, supra:

TABLE IV

HEADSPACE CONSTITUENTS OF NUTMEG OIL

Compound	% After 15 Min.	% After 1 Hour	% After 24 Hours
α-Thujene	2.80	2.90	2.30
α-Pinene	25.00	25.20	20.50
Camphene	0.40	0.40	0.32
Sabinene	25.20	24.40	21.00
β-Pinene	20.00	18.90	16.50
Myrcene	2.80	3.00	3.00
α-Phellandrene	1.00	1.00	1.10
Δ-3 Carene	1.00	1.00	1.00
α-Terpinene	3.80	4.10	4.40
P-cymene	1.30	1.40	1.41
Limonene	6.60	7.30	8.00
γ-Terpinene	4.50	5.10	6.80
Terpinolene	1.20	1.40	2.20
Linalool	Trace	Trace	0.50
Terpineol-4	1.80	2.30	6.81
α-Terpineol	Trace	0.20	0.60
Safrole	0.20	0.30	1.40
Myristicin	Trace	0.10	0.75

For the purpose of the dose calculations, the head space concentrations of myristicin was assumed to be 0.1% of the total nutmeg oil that had evaporated.

Table V summarizes the percent myristicin in the vapor in equilibrium with nutmeg oil or in equilibrium with mace extract after 15 minutes, 1 hour, 2 hours, 3 hours, 4 hours and 24 hours. The analytical procedure for the determination was described previously in this example.

It has been found that neat Nutmeg Oil East Indian contains 7.10% myristicin and mace extract contains 31.00% myristicin.

TABLE V

HEAD SPACE STUDY OF NUTMEG AND MACE

EVAPORATION TIME	% MYRISTICIN IN THE VAPOR OVER NUTMEG	% MYRISTICIN IN THE VAPOR OVER MACE EXTRACT
15 Minutes	Trace	Trace
1 Hour	0.10	0.90
2 Hours	0.40	2.80
3 Hours	0.50	5.00
4 Hours	0.60	7.00
24 Hours	0.75	8.00

Table VI sets forth overall compositions of Nutmeg Oil East Indian, Nutmeg Oil Terpenless and two other commercial nutmeg oils as well as Mace Extract:

TABLE VI

CONSTITUENTS OF NUTMEG AND MACE OIL

Compound	NUTMEG OIL EAST INDIAN	NUTMEG OIL TERPENLESS	COMMERCIAL NUTMEG OIL SAMPLE X	COMMERCIAL NUTMEG OIL SAMPLE Y	MACE EXTRACT
α-Thujene	2.50%	1.00%	1.50%	0.60%	0.60%
α-Pinene	22.20	9.10	30.70	0.76	1.10
Camphene	0.30	0.15	0.43	Trace	-
Sabinene	18.73	14.60	16.55	0.60	1.10
β-Pinene	15.30	11.61	12.00	1.80	2.63
Myrcene	2.50	2.70	2.00	0.50	0.74
α-Ph llandrene	0.94	1.10	0.40	0.18	0.25
Δ-3-Carene	0.90	0.98	0.45	1.40	0.67
α-Terpinene	3.70	4.60	1.64	2.30	1.30
p-Cymene	1.00	1.74	1.72	-	1.50
Limonene	6.60	9.40	17.63	2.90	3.00
γ-Terpinene	5.50	8.92	2.40	2.10	2.20
Trans-Sabinene Hydrate	0.20	0.33	0.34	1.33	1.15
α-p-Dimethyl Styrene	0.07	0.12	Trace	Trace	0.10
Terpinolene	1.77	3.00	0.85	0.75	1.20
Cis-Sabinene Hydrate	0.15	0.30	0.20	0.80	0.80
Linalool	0.19	0.30	0.20	0.80	0.80
Unknown (Two Isomers)	-	-	-	2.30	4.00

TABLE VI (con't)

CONSTITUENTS OF NUTMEG AND MACE OIL

Compound	NUTMEG OIL EAST INDIAN	NUTMEG OIL TERPENLESS	COMMERCIAL NUTMEG OIL SAMPLE X	COMMERCIAL NUTMEG OIL SAMPLE Y	MACE EXTRACT
2-p-Menthen-1-ol	0.14	0.25	0.16	Trace	Trac
2-p-Menthen-1-ol (Isomer)	0.09	0.18	0.10	1.14	Trace
2-Ethyl-5-Methyl Furan	Trace	Trace	Trace	-	-
Terpineol-4	6.00	10.48	3.58	6.30	3.61
α-Terpineol	0.70	1.28	0.47	0.70	0.60
Piperitol	Trace	Trace	Trace	Trace	Trace
Piperitol (Isomer)	Trace	Trace	Trace	Trace	Trace
p-Menth-1-en-4-yl-Ethyl Ester	-	-	-	0.60	1.50
Saffole	1.70	3.00	1.12	3.64	4.45
Iso Bornyl Acetate	-	-	-	Trace	Trace
B rnyl Acetate	Trace	0.13	Trace	Trace	Trace
Thymol	-	-	-	Trace	-
Amyl Anisole (T)	0.21	0.36	Trace	Trace	-
Eugenol	0.21	0.36	0.10	0.80	1.00
α-Terpinyl Acetate	0.10	0.20	0.05	0.10	0.30
α-Cubebene	0.05	0.10	Trace	0.10	Trace
Vanillian	-	-	-	Trace	-

TABLE VI (con't)

CONSTITUENTS OF NUTMEG AND MACE OIL

Compound	NUTMEG OIL EAST INDIAN	NUTMEG OIL TERPENLESS	COMMERCIAL NUTMEG OIL SAMPLE X	COMMERCIAL NUTMEG OIL SAMPLE Y	MACE EXTRACT
Neryl Acetate	0.10	0.17	0.08	0.10	Trace
Euganyl Methyl Ether	0.30	0.50	0.10	1.80	1.80
α-C paene	0.23	0.41	0.16	0.93	0.55
Trans Iso Eugenol	0.31	0.60	Trace	0.71	3.30
α-Bergamotene	Trace	0.12	Trace	Trace	Trace
Methyl Iso Eugenol	Trace	Trace	Trace	0.35	0.26
Myristicin	7.10	11.23	5.00	33.50	31.00
A-Cadinene	Trace	Trace	Trace	Trace	0.10
Elemicin	0.11	0.45	0.07	1.85	1.20
Dodecanoic Acid	-	-	-	Trace	-
4-Allyl 2,6-Dimethoxy Phenol	0.08	0.19	Trace	2.70	5.00
Myristic Acid	-	-	-	15.32	-
Ethyl Tetradeconate	-	-	-	5.10	2.30
M thyl Octadeconate	-	-	-	0.85	1.00
Ethyl Palmitate	-	-	-	1.30	5.00
Ethyl Oleate	-	-	-	-	1.50
Octadecenoic Acid Methyl Ester	-	-	-	1.00	-
	99.98	99.96	100.00	98.01	87.64

Trace - CO.01%

EXAMPLE I(C)

ISOLATION OF ELEMICIN FROM OIL OF ELEMI

Elemicin was separated from Oil of Elemi using the following procedure:

Elemi Oil (Contains 7% Elemol and 3% Elemicin)

↓ Distillation

Enriched Fractions (Elemol 70% and Elemicin 30%)

↓ Dehydration of Elemol

Sesquiterpenes (70% and Elemicin 30%)

↓ Column Chromatography

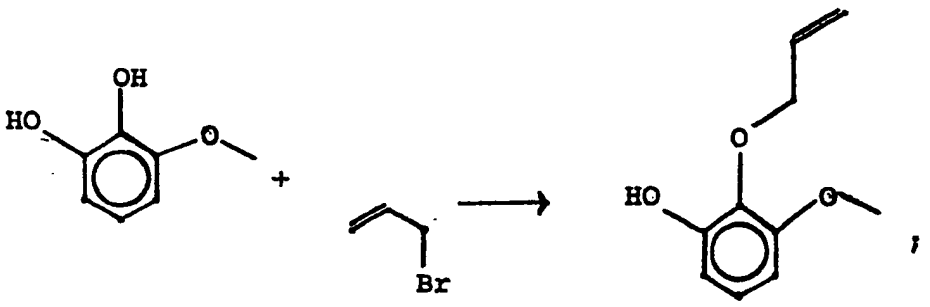
Sesquiterpenes Elemicin —Dist.→ 94% Elemicin

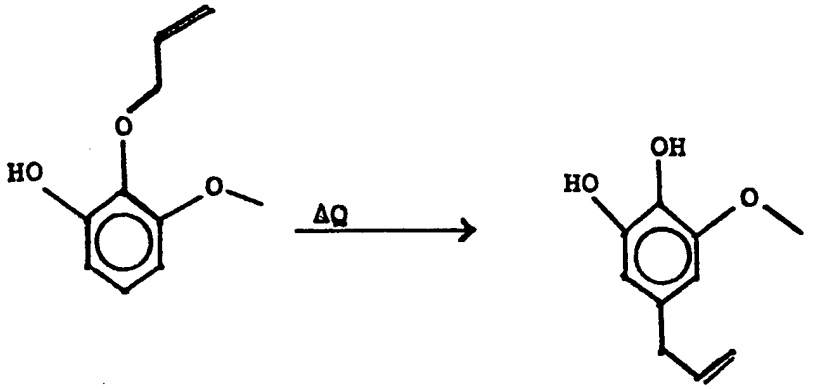
The 94% Elemicin is used in subsequent Examples V, et seq.

EXAMPLE I(D)

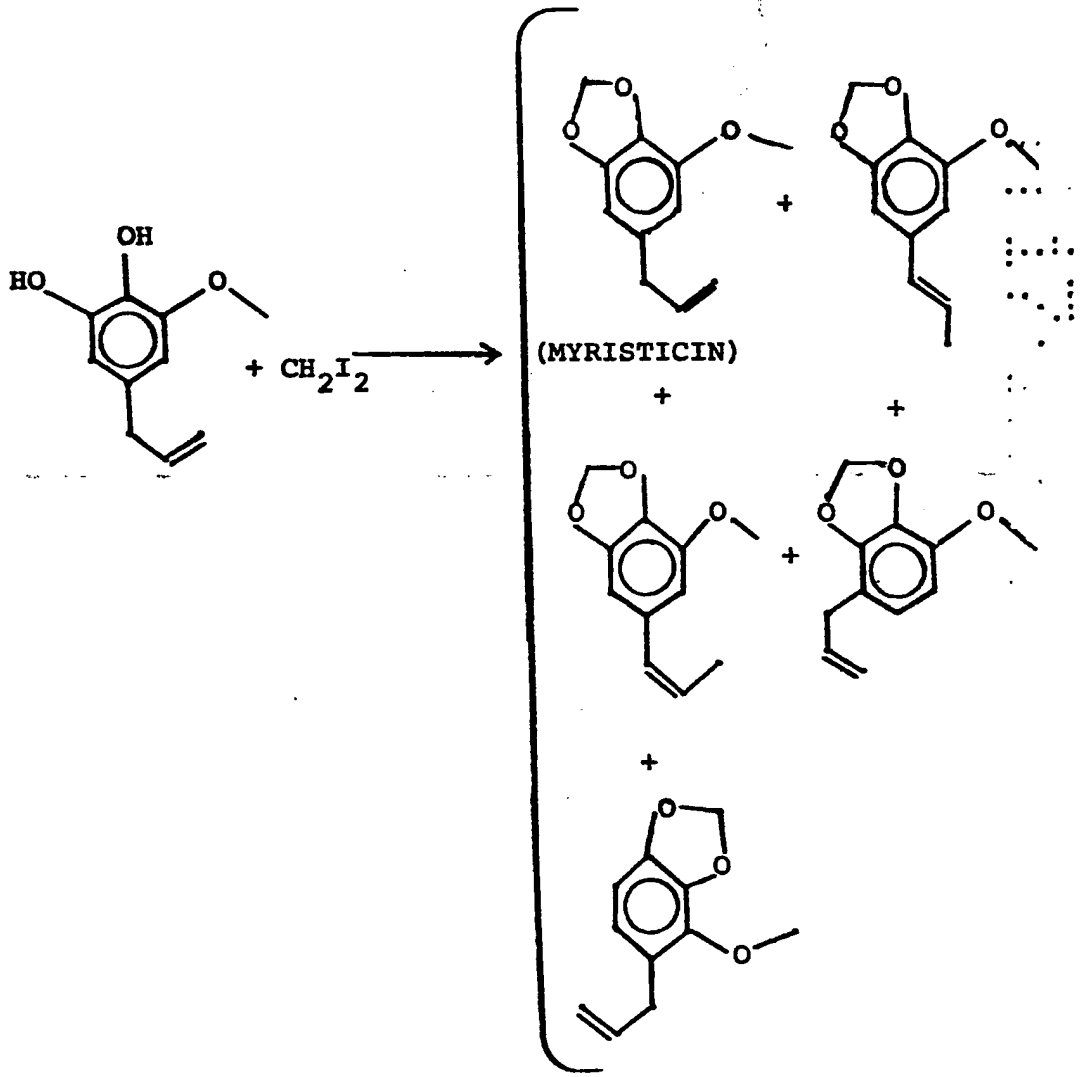
MYRISTICIN SYNTHESIS

Myristicin for use in subsequent Examples II, et seq, was synthesized using as a precursor, 1,2-dihydroxy-3-methoxy benzene according to the following reaction sequence:





; and



The isolated myristicin was us d in Examples V, et seq.

EXAMPLE II

Four odorant conditions were tested using a factorial experimetal design. Analysis of the results was by a two way analysis of variance. Factors were Fragrance "A" and "Neutral" Fragrance and levels were +/- the presence of "actives". Analysis of the results was with the BMDP statistical package and a Digital Equipment Co. (DEC) 11/780 VAX computer. An explanation of the analysis of variance (ANOVA) technique is found in:

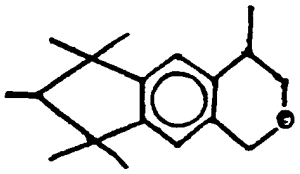
R.B. McCall, "Fundamental Statistics for Psychology," 2nd Ed., Harcourt Brace Jovanovich,, New York, N.Y.; 1975, pages 236-64.

The term "p" is the significance level as obtained from the "F" test applied to the ANOVA results. "p" Is the probability that the results obtained are due to random error.

The composition of the fragrances was as follows:

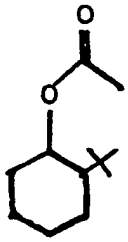
1. Fragrance "A" composition:

GALAXOLIDE® [Registered Trademark of International Flavors & Fragrances Inc.: a tricyclic isochroman having the structure:



] 47.1%

Verdox [a chemical manufactured by International Flavors & Fragrances Inc. having the structure:



] 21.1%

Diethyl Phthalate.....12.6%

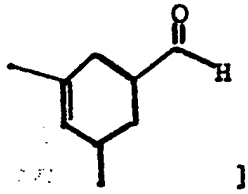
Peach Aldehyde Coeur.....10.5%

Prenyl Acetate.....4.0%

Hexyl Cinnamic Aldehyde..... 2.6%

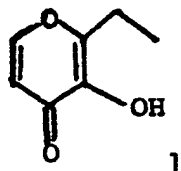
Iso Amyl Butyrate..... 1.3%

Aldehyde AA-Triplal [a specialty manufactured by International Flavors & Fragrances Inc. having the structure:



].....0.05%

Veltol Plus [ethyl maltol having the structure:



].....0.01%

2. "Actives" composition:

Nutmeg Oil East Indian.....97.10%

Mace Extract..... 0.14%

Neroli Oil..... 0.98%

Diethyl Phthalate..... 0.44%

Valerian Oil Indian..... 0.05%

3. Fragrance + Active:

Fragrance "A"..... 60.0%

"Actives"..... 40.0%

4. "Neutral" Fragrance:

Diethyl Phthalate.....100.0%

5. "Neutral" Fragrance + "Actives":

Diethyl Phthalate..... 50.0%

Fragrance "A"..... 10.0%

"Actives"..... 40.0%

The subjects used for the study were drawn from the New Haven, Connecticut area. One hundred and tw nty subjects were used for the experiment or thirty subjects for each of the four cells. The study was run double blind. Subjects were run at one at a time and the script was presented by tape recorder. Blood pressures and heart rates were measured with an autoinflatable, printing, digital sphygmomanometer manufactured by the Takeda Medical Co., Inc. of Tokyo, Japan.

The protocol allowed for investigation of the cardiovascular and mood responses to a stressor with and without "fragrance" or stress reactivity reducer (SRR) treatments. The objective was to provide a stressor that would produce a stress type and level similar to that experienced in the work place. A further objective was to measure both blood pressure and mood changes during the stress period since the literature has shown that reactivity to stress correlates with disease. The protocol was as follows:

1. Attachment of the blood pressure cuff.
2. Questionnaire.
3. Stress I:
   (a) baseline
   (b) mood self report
   (c) 6 low stress questions (LS1)
   (d) mood self report
   (e) 6 mild stress questions (MS1)
   (f) mood self report
   (g) baseline
   (h) mood self report
4. Treatment:
   (a) Fragrance "A" or
   (b) Fragrance "A" + "Actives" or
   (c) "Neutral" Fragrance or
   (d) "Neutral" Fragrance + "Actives"
5. Stress II:
   (a) baseline

(b) mood self report

(c) 6 low str ss questions (LS2)

(d) mood self r port

(e) 6 mild stress questions (MS2)

(f) mood self report

(g) base line

(h) mood self report

6. Post-experimental questionnaire

7. Removal of recording devices and debriefing.

The initial questionnaire contained 53 true/false questions taken from the Marlowe-Crowne repression test and the bending form of the Taylor Anxiety Scale. It was used to classify subjects on the basis of repression and anxiety.

Baseline periods involved the subject sitting still, resting. Mood self reports were made by the subject reporting by means of a seven point scale (0-6) his or her degree of relaxation, anger, anxiety, happiness, tenseness, embarrassment, calmness, fear and sleepiness. Neutral and mild stress questions were taken from the Phase Association Test:

Mandler, et al, "Response to Threat: Relations Among Verbal and Physiological Findings" (Psychological Monographs, 1961, Vol. 75, No. 9).

Subjects were asked to respond as quickly as possible with the first phrase that came to mind following presentation of a stimulus phrase. Neutral questions included "My name is?" Stress phrases included: "The thing I like least about myself is..." and "If may child were dating someone of a difference race I would...".

During the treatment period the subject smelled one of the fragrances or postulated stress reactivity reducing agents from a "Measuring Line" style perfume blotter obtained from Frank Orlandi, Inc.: 31-02 Northern Boulevard, Long Island City, Queens, New York 11101. The blotter was about 15 cm long by about 1.4 cm wide. It was dipp d into a 20% solution of fragrance and/or postu-

lated stress reactivity r ducing agent in ethyl alcohol to a level of about 2 cm (the second red lin), all wed to dry for five minutes and then positioned about 6 cm from th subject's nose.

The final questionnaire asked for the subject's reactions to the experiment.

The analysis of variance of the results showed significant changes in systolic blood pressure and self reports for the subjects smelling either fragrance "A" plus "actives" or "neutral" fragrance plus "actives" versus the subjects smelling the fragrance "A" or the "neutral" fragrance alone.

The changes deemed to be relevant to the every day stress and strain of life were the blood pressure and mood changes due to the stress questions relative to the low stress questions (MS - LS); (see the protocol for definitions of MS and LS). To obtain a Change score for a particular condition the changes before and after the condition were compared thusly:

Change due to the fragrance "A" or "neutral" fragrance = N; and N = (MS2 - LS2) - (MS1 - LS1).

In the same way a change score can be calculated for the fragrance "A" plus "actives" or the "neutral" fragrance plus "actives". This change is referred to as "A".

To obtain the effect of one condition relative to another the change score for one condition can be subtracted from that for another. Thus, the "actives" effect is: (A - N).

For Table VII presented below, the "actives" effect was obtained by pooling the results for the fragrance "A" plus "actives" and "neutral" plus "actives" to obtain "A" and pooling the results for the fragrance "A" and "neutral" fragrances to obtain "N".

In the analysis of variance treatment of the results, the Change score presented below in Table VII is numerically equal to the period by trial by "actives" three-way interactions. In this context, "p riod" is

the average of the effects after treatment relative to the effects before treatment: (LS2 + MS2) - (LS1 + MS1) averaged across all four treatments. "Trial" is the average of the effects due to mild stress relative to those due to low stress: (MS1 + MS2) - (LS1 + LS2) averaged across all treatments. "Actives" is the average of effects for the compositions containing "actives" relative to effects for the compositions containing no "actives": (LS1 + LS2 + MS1 + MS2) averaged across fragrance "A" + "actives" and neutral fragrance + "actives" minus (LS1 + LS2 + MS1 + MS2) averaged across fragrance "A" and the neutral fragrance.

TABLE VII

EFFECT OF "ACTIVES" ON MILD STRESS

VARIABLE	CHANGE ("A" - N)	SIGNIFICANCE LEVEL (p)
Systolic Blood Pressure	-4 mm/Hg.	0.08
Calmness	0.77	0.01
Embarrassment	-2.31	0.03
Happiness	0.77	0.0003
Anger	-0.51	0.03

Thus, the presence of "actives" in either the fragrance "A" or the "neutral" fragrance decreases systolic blood pressure; increases calmness; decreases embarrassment; increases happiness; and decreases anger.

Even though the subjective results in this case have been quantified, it is important to point out that they also correlated with the systolic blood pressure change.

EXAMPLE III(A)

Two odorant conditions were tested using a factorial experimental design. Analysis of the results by a one way analysis of variance was done. The factor was "fragrance" or "postulated stress reactivity reducing agent"; the levels were plus and minus "actives". The details of the statistical analysis techniques are presented in Example II, supra.

The substances tested were fragrance "A" and a composition of matter composed only of "actives". The composition of the fragrance "A" and of the "actives" are presented in Example II, supra.

The subjects used for the study were drawn from the Union Beach, New Jersey area (Monmouth County in the State of New Jersey). Fourteen subjects were used for the study; seven in each of the two cells. The script was presented by tape recorder and blood pressures were measured with a recording automatic sphygmomanometer as described in Example II, supra. The experimental session periods were the following:

1. Attachment of the blood pressure cuff.
2. Questionnaire.
3. Stress I:
   (a) baseline (BL)
   (b) mood self report
   (c) 6 low stress questions (LS1)
   (d) mood self report
   (e) 6 mild stress questions (MS1)
   (f) mood self report.
4. Treatment:
   (a) fragrance "A" (F) or
   (b) actives fragrance (F).
5. Stress II:
   (a) mood self report
   (b) 6 low stress questions (LS2)
   (c) mood self report
   (d) 6 mild stress questions (MS2)

(e) mood s lf report

(f) bas line (BL2).

6. Post-experimental questionnaire.

7. Removal of recording devices and debriefing.

Details of the parts of the protocol are set forth in Example II, supra. During the treatment period the subjects smelled one of the fragrances or postulated stress reactivity reducing agents from a one dram vial containing a wick saturated with a solution made up of 60% test substance and 40% food grade ethyl alcohol.

The experiment was designed to show the effect of the stressor and (i) fragrance or (ii) stress reactivity reducing agent on systolic blood pressure. The stressor is designed to be mildy frustrating and tension producing. The subject does not have adequate time to answer the questions which are controversial and have complex answers.

Figure 3 shows the change in systolic blood pressure during the periods of the protocol. For the "before fragrance" or "stress reactivity reducing agent" periods, the moderate stress questions produce about a 5 mm/Hg rise in blood pressure relative to the low stress questions (MS1 - LS1). In the after "fragrance" or "stress reactivity reducing agent" periods, the subjects smelling the "actives" experience a 1 mm/Hg decrease in systolic blood pressure during the moderate stress questions relative to the low stress questions while the subjects smelling fragrance "A" experience an 8 mm/Hg increase during the same period (MS2 - LS2). The change for the "actives" group relative to the fragrance "A" group as follows:

"Actives" Group:

A = (MS2 - LS2) - (MS1 - LS1) = -1 - 5 = -6 mm/Hg

Non-Actives Group:

N = (MS2 - LS2) - (MS1 - LS1) = 8 - 5 = 3 mm/Hg

Change:

A - N = -6 -3 = -9 mm/Hg (p = 0.03).

Th Change score shows that th "Activ s"

decreases systolic blood pressure during a mildly frustrating event which has been shown in the first part of the experiment to increase systolic blood pressure. The fragrance "A" does not exhibit this effect.

EXAMPLE III(B)

A preferred odorant composition was tested on a 73 year old male subject. The composition of the odorant was 60% fragrance "A" and 40% "actives" (see Example II, supra). The mode of administration was by means of the vial-wick system as described in Example III, supra. The testing protocol was the one described in Example III, supra, and the protocol periods (BL1, LS1, MS1, F, LS2, MS2 and BL2) are also described in Example III. Figure 4 shows the subject's systolic blood pressure in mm/Hg for each of the periods (indicated by reference numeral 81). The shape of the graph is similar to that for the graph for the "actives" groups (indicated by reference numeral 72) presented in Figure 3. Of particular interest are systolic blood pressure changes between LS1 and MS1 and LS2 and MS2. The subject experienced a 6mm/Hg increase in systolic blood pressure (MS1 - LS1) for the "before fragrance" periods whereas he experienced an 8mm/Hg decrease (MS2 - LS2) for the same periods after the odorant-conditioning period. Hence the Change score (see Example III, supra) is the following:

$$A = (MS2 - MS1) - (MS1 - LS1) = -8 - 6 = -14mm/Hg.$$

This example further shows that the "actives" composition lowers a human's reaction to stress.

EXAMPLE IV(A)

Two odorant conditions were tested using a factorial experimental design. Analysis of the results by a one way analysis of variance was done. The factor was ["fragrance" or postulated stress reactivity reducing "agent"]; the levels were plus and minus "actives". The details of the statistical analysis techniques are pr -

sented in Example II, supra.

Th substances tested wer a composition of matt r compos d of Ethanol/Distilled Water and a composition of matter composed of Ethanol/"actives". The composition of the "actives" is presented in Example II, supra.

The subjects used for the study were drawn from the Union Beach, New Jersey area (Monmouth County in the State of New Jersey). Thirty subjects were used for the study: fifteen in each of the two cells. The script was presented by tape recorder and blood pressures were measured with a recording automatic sphygmomanometer as described in Example II, supra. The experimental session periods were the following:

1. Attachment of the blood pressure cuff.
2. Questionnaire.
3. Stress I:
   (a) Baseline (BL1)
   (b) mood self report
   (c) 12 mild stress questions (VB1).
   (d) mood self report
   (e) serial counting exercise (MB1)
   (f) mood self report
4. Treatment:
   (a) Ethanol/Water (E) or
   (b) Ethanol/Actives (E+)
5. Stress II:
   (a) Baseline (BL2)
   (b) mood self report
   (c) 12 mild stress questions (VB2)
   (d) mood self report
   (e) serial counting exercise (MB2)
   (f) mood self report
6. Post-experimental questionnaire.
7. Removal of recording devices and debriefing.

The initial questionnaires consist of practic mood valuations and a number of other questionnaires

unrelated to the main experiment.

Baseline periods involved the subject sitting still, resting. The mood self reports were made by th subject reporting by means of a nine point scale (0-9) his or her degree of relaxation, anger, anxiety, happiness, tenseness, embarrassment, calmness, boredom, and excitement. The mild stress questions are as set forth in Example II, supra. The serial counting exercise consisted of asking subjects to write down their responses to a series of instructions such as "count forward from zero by fives". The subjects were informed that they would be given a bonus based on the number of correct operations they performed.

Starting at the beginning of the treatment period, the subjects smelled a fragrance or postulated stress reactivity reducing agents from a one dram vial containing a wool wick saturated with a solution made up of 60% test substance and 40% food grade ethyl alcohol. They continued smelling this fragrance through the end of stress II.

This protocol was designed to be somewhat more stressful than that set forth in Example II, supra. The "serial counting" is designed to be a measured performance task.

The post-experiment questionnaires consisted of the Marlowe-Growne/Taylor Anxiety Scale and a questionnaire regarding the subject's reaction to the experiment as set out in Example II, supra.

Two sets of "change scores" are calculated for this experiment in the same manner as set out in Examples II and III, supra. The first is the difference between the baseline and verbal stress values and the second is the difference between the baseline and mathematical stress values as follows:

VB change = (VS2 - BS2) - (VS1 - BS1)

MB change = (MS2 - BS2) - (MS1 - BS1)

The ff ct was then calculated as the diff rence betwe n the chang score for the "active" and that of water.

The significance is d termined by thre -way analysis of varianc as set forth in Example II, supra.

Table VIII

Effect of "Actives" on Stress

Variable	VB change	Significance Level (p)	MB change	Significance Level (p)
Systolic BP	-6.2 mm/Hg	0.03	-1.5 mm/Hg	0.62
Diastolic BP	-6.7 mm/Hg	0.05	-6.4 mm/Hg	0.09
Relaxed	1.1	0.11	1.6	0.04
Anxious	-1.1	0.12	-3.1	0.002
Tense	-1.6	0.08	-2.3	0.06
Embarrassed	-0.7	0.45	-1.5	0.04
Bored	1.9	0.06	2.4	0.06

While the level of significance varies between the stressors, the presence of "active" reduces both systolic and diastolic blood pressure; increases relaxation; increases boredom; decreases anxiety; decreases tension and decreases embarrassment.

EXAMPLE IV(B)

Two odorant conditions were tested as set forth in Example IV(A), supra. The treatments tested were fragrance "A" and fragrance ("A" + "actives"). The composition of these is as set forth in Example II, supra.

The subjects used for the study were drawn from the Union Beach, New Jersey area (Monmouth County in the State of New Jersey). Thirty-five subjects were used for the study: nineteen received fragrance "A" and sixteen fragrance ("A" + "actives").

The change scores and statistical confidences levels were calculated as set forth in Example IV(A). The effect was then calculated as the difference between the change score for ("A" + "actives") and that of "A" alone.

Table IX

Effect of "A"+"Actives" on Stress

Variable	VB change	Significance Level (p)	MB change	Significance Level (p)
Systolic BP	-2.6 mm/Hg	0.39	-5.2 mm/Hg	0.18
Diastolic BP	-1.5 mm/Hg	0.49	-7.2 mm/Hg	0.04
Anger	-1.0	0.05	-1.0	0.05
Anxiety	-1.2	0.04	-0.3	0.70
Happy	0.8	0.27	1.1	0.13
Tense	-2.0	0.04	-1.5	0.13

Thus, the presence of "actives" reduces blood pressure; increase happiness; reduces anxiety; reduces tension and reduces anger. This example further shows how the "actives" reduce human stress.

EXAMPLE IV(C)

Two odorant conditions were tested as set forth in Example IV(A), supra. The treatments tested were fragrance "F" and fragrance ("F" + "actives"). The composition of these is as follows:

1. Fragrance "F" Composition:

Isobornyl acetate	19.42%
Cedarwood oil	20.65%
Bornyl acetate	6.75%
Pine oil	6.50%
Hexalydro-4,7-methanoindan-5 (or 6)-yl propionate	3.50%
Ethyl acetoacetate	2.50%
α-Terpeneol	2.38%
Methyl nonylacetaldehyde	1.56%
Linalool	1.62%
Coumarin	1.25%
Dipropylene glycol	33.86%

2. Fragrance "F" + "Actives":

Fragrance "F"	60.00%
Actives (Example II, supra)	40.00%

The subjects used for the study were drawn from the Union Beach, New Jersey area (Monmouth County in the State of New Jersey). Sixty-fiv subj cts were

used for th study: thirty-three received fragranc "F" and thirty-two fragrance ("F" + "Actives").

The change scores and statistical confidences levels were calculated as set forth in Example IV(A). The effect was then calculated as the difference between the change score for ("F" + "Actives") and that of "F" alone.

Table IX

Effect of "F"+"Actives" on Stress

Variable	VB change	Significance Level (p)	MB change	Significance Level (p)
Systolic BP	-3.1 mm/Hg	0.20	-3.2 mm/Hg	0.16
Diastolic BP	-4.0 mm/Hg	0.03	-4.5 mm/Hg	0.04
Calm	1.4	0.04	1.7	0.04

Thus, the presence of "actives" reduces blood pressure and increase calmness.

EXAMPLE V

Experiments covered by Examples II, III and IV are carried out using in place of the "Actives" composition the following substantially pure materials:

(i) Nutmeg Oil East Indian;
(ii) Neroli Oil;
(iii) Mace Extract;
(iv) Valerian Oil;
(v) Myristicin;
(vi) Elemicin; and
(vii) Isoelemicin.

Results substantially the same as those obtained in Examples II, III and IV are obtained when using the foregoing pure materials instead of the "actives".

In the following Examples VI, et seq, the following materials are used in perfumed articles causing use of these perfumed articles to create mild stress reactivity reducing effects on the user:

TABLE XI

(i) "Actives" composition of Example II;
(ii) Nutmeg Oil East Indian substantially pure;

(iii) Mace Extract substantially pure;

(iv) Neroli Oil;

(v) Valerian Oil;

(vi) Myristicin;

(vii) Elemicin; and

(viii) Isoelemicin.

EXAMPLE VI

PREPARATION OF A COSMETIC POWDER COMPOSITION

A cosmetic powder is prepared by mixing in a ball mill 100 grams of talcum powder with 0.25 grams of each of the compositions of Table VIII, supra. Each of the cosmetic powders prepared with each of the ingredients of the compositions of matter set forth in Table VIII, supra, creates an effect which can be described as "stress reactivity reducing" in the user.

When each of items (i)-(viii) taken alone is combined at a 50:50 (weight:weight) level with fragrance "A" a pleasant apple aroma is imparted to the cosmetic powder.

EXAMPLE VII

PREPARATION OF A COLOGNE AND HANDKERCHIEF PERFUME

Each of the compositions of matter of Table VIII, supra, are incorporated into colognes at concentrations of 2.0%, 2.5%, 3.0%, 3.5%, 4.0%, 4.5% and 5.0% in 95% aqueous ethanol together with 4.0%, 4.5% and 5.0% of fragrance "A" of Example II; and into handkerchief perfumes at concentrations of 15%, 20%, 25%, 30% and 40% in 95% aqueous ethanol together with 10% by weight of fragrance "A" of Example II. Distinctive apple aromas are imparted to each of the colognes and handkerchief perfumes and each of the colognes and handkerchief perfumes gives rise to a "stress reactivity-reducing" effect on the user.

EXAMPLE VIII

DEODORANT STICK

A deodorant stick composition is prepared containing the following materials:

INGREDIENTS	PARTS BY WEIGHT
Propylene Glycol	68.00
Sodium Stearate	7.00
Distilled Water	23.75
IRGASAN® DP-300 (2,4,4-trichloro-2'-hydroxy diphenyl ether, manufactured by the Ciba-Geigy Chemical Co. and a Trademark of the Ciba-Geigy Chemical Co.)	0.25
Composition containing fragrance "A" (50 parts by weight) and one of items (i)-(viii) of Table VIII, supra, (50 parts by weight)	1.00

The ingredients are combined without "active" substance/fragrance composition and heated to 75°C. These ingredients are mixed and continued to be heated until the sodium stearate has dissolved. The resulting mixture is cooled to 40°C. and the "active" substance/fragrance composition (containing one of the stress reactivity reduction substances of Table VIII, supra) is added and mixed at 40°C. until a suspension is formed.

The resulting suspension is formed into deodorant sticks. On use thereof, users subjected to stress conditions experience reduction in physiological and/or subjective reactivity to stress.

EXAMPLE IX

SOLID ROOM DEODORANT COMPOSITION

A solid room deodorant composition is prepared as follows:

INGREDIENTS	PARTS BY WEIGHT
PART A:	
Distilled Water	88.45
GELCARIN AFG 15 (Marine Colloids)(1)	3.00
Formaldehyde	0.05
PART B:	
Glycerine	3.50
PART C:	
Composition containing fragrance "A" (50 parts by weight) and one of items (i)-(viii) of Table VIII, supra (50 parts by weight)	1.00
PART D:	
TWEEN 80 (ICI Americas)(2)	4.00

The composition is prepared by:

1. Heating the water to 85°C. and dispersing the GELCARIN AFG 15 therein;
2. Slowly adding the glycerin while maintaining the mixture at 85°C.;
3. Combining the TWEEN 80 and composition containing "actives" and fragrance;
4. Adding the TWEEN/(fragrance plus "actives") composition to the resulting mixture;
5. Adding formaldehyde to the resulting mixture; and
6. Pouring the resulting mixture into a mold.

The contents are allowed to cool, the mold is opened and the solid "cakes" are removed. The "cakes" are plac d into standard air deodorizing apparatus.

On op ration of the standard air d odorizing

apparatus as a room deodoriz r, after four minutes, th room has an a sth tically pl asing apple aroma and further, a person placed in said room who is subject to stress conditions will have a significant stress reactivity reduction.

Notes: 1. GELCARIN AFG 15 is Carageenan manufactured by Marine Colloids, Inc. Division of FMC Corporation of Springfield, New Jersey 07081.

2. TWEEN 80 is Polysorbate 80 otherwise known as (polyethylene glycol)$_6$-Sorbitan Oleate, manufactured by ICI Americas Inc. of Wilmington, Delaware 19897.

EXAMPLE X

BODY OIL COMPOSITION

A body oil composition is prepared as follows:

INGREDIENTS	PART BY WEIGHT
Mineral Oil [KLEAROL® (Witco)]	45.0
Isopropyl Myristate	50.0
Composition containing fragrance "A" (50 parts by weight) and one of items (i)-(viii) of Table VIII, supra (50 parts by weight)	5.0

The composition of this example is prepared by combining the ingredients with mixing, aging and filtering.

Each of the body oil preparations prepared with each of the ingredients of the compositions of matter set forth in Table VIII, supra, creates an effect which can be described as "stress reactivity-reducing" in the user. In addition, a pleasant apple aroma is imparted to the user in ach case.

EXAMPLE XI

HOT OIL TREATMENT COMPOSITION (FOR HAIR)

A hot oil treatment composition for hair is prepared as follows:

PARTS BY WEIGHT	INGREDIENTS
65.9	UCON Lubricant 50-HB-660[1] (Union Carbide)
30.0	UCON Lubricant 50-HB-400[2] (Union Carbide)
3.0	LANTROL AWS (Emery)[3]
0.1	Propyl Paraben
1.0	Compositions containing fragrance "A" (50 parts by weight) and one of items (i)-(viii) of Table VIII, supra (50 parts by weight)

The composition of this example is prepared by simply adding the ingredients in order while mixing.

Each of the resulting hot oil treatment compositions prepared with each of the ingredients of the compositions of matter set forth in Table VIII, supra, creates an effect which can be described as "stress reactivity-reducing" in the user. In addition, a pleasant apple aroma is imparted to the user.

Notes:

1. UCON Lubricant 50-HB-660 is (polypropylene glycol)$_{12}$—butyl ether manufactured by the Union Carbide Corporation of Danbury, Connecticut 06817.
2. UCON Lubricant 50-HB-400 is (polypropylene glycol)$_{9}$-butyl ether manufactured by the Union Carbide Corporation of Danbury, Connecticut 06817.
3. LANTROL AWS is a water dispersable alkoxylated Lanolin oil marketed by Emery Industries of Cincinnati, Ohio 45202.

EXAMPLE XII

AEROSOL ROOM SPRAY COMPOSITION

An aerosol room spray composition is prepared as follows:

INGREDIENTS	PARTS BY WEIGHT
SPAN 80[1]	1.00
Composition containing fragrance "A" (50 parts by weight) and one of items (i) — (viii) of Table VIII, supra (50 parts by weight)	0.25
Distilled Water	68.75
Propellant A-46[2]	30.00

An aerosol room spray is prepared as follows:

1. adding the water to an aerosol container;
2. mixing the composition containing fragrance "A" and "actives" and the SPAN 80;
3. adding the fragrance/"actives"/SPAN 80 composition to the container;
4. crimping on an aerosol valve;
5. pressurizing the container with Propellant A-46; and
6. fitting an actuator to the valve.

When the resulting composition is sprayed from the aerosol container into a 20' x 20' x 10' normally ventilated room (T=65°F.), after four minutes, the room has an aesthetically pleasing apple aroma and, further, a person placed in said room who is subjected to stress conditions will have a significant stress reactivity reduction.

Notes:

1. SPAN 80 is Sorbitan Oleate, manufactured by ICI Americas Inc., of Wilmington, Delaware 19897.
2. Propellant A-46 is a mixtur of 85 w ight percent isobutane and 15 weight percent propan .

CLAIMS

1. A composition comprising nutm g oil, mace extract, neroli oil, valerian oil, myristicin, elemicin and/or isoelemicin for use in reduction of physiological and/or subjective reactivity to stress in human beings.

2. Use of a composition comprising nutmeg oil, mace extract, neroli oil, valerian, myristicin, elemicin and/or isoelemicin oil for the reduction of physiological and/or subjective reactivity to stress in human beings.

3. Use of nutmeg oil, mace extract, neroli oil, valerian oil, myristicin, elemicin and/or isoelemicin for preparing a composition for treatment of physiological and/or subjective reactivity to stress.

4. The method of causing the reduction of physiological and/or subjective reactivity to stress in a human being subjected to stress which comprises administering to said human transdermally or through inhalation an effective amount of a stress reactivity-reducing substance selected from the group consisting of:

Nutmeg Oil;

Mace Extract;

Neroli Oil; and

Valerian Oil.

5. The method of claim 4, wherein the stress reactivity-reducing substance is nutmeg oil and the amount administered is in the range of from about 13 micrograms up to about 1000 micrograms.

6. The method of causing the reduction of physiological and/or subjective reactivity to stress in a human being subjected to stress which comprises administering to said human transdermally or through inhalation an effective amount of a composition of matter consisting essentially of:

(a) a stress reactivity-reducing substance selected from the group consisting of:

Nutmeg Oil;
Mace Extract;
Neroli Oil; and
Valerian Oil;

and (b) a carrier perfume composition compatible with said stress reactivity-reducing substance

the weight ratio of said stress reactivity-reducing substance to said carrier perfume composition being in the range of from about 1:100 up to about 100:1.

7. The method of claim 6, wherein the stress reactivity-reducing substance is nutmeg oil and the amount administered is in the range of from about 13 micrograms up to about 1000 micrograms.

8. The method of causing the reduction of physiological and/or subjective reactivity to stress in a human being subjected to stress which comprises administering to said human transdermally or through inhalation an effective amount of a composition of matter consisting essentially of:

(a) a stress reactivity-reducing substance selected from the group consisting of:
Nutmeg Oil;
Mace Extract;
Neroli Oil; and
Valerian Oil;

and (b) ethyl alcohol,

the weight ratio of said stress reactivity-reducing substance to said ethyl alcohol being in the range of from about 1:99 up to about 99:1.

9. The process of claim 8, wherein the stress reactivity-reducing substance is nutmeg oil and the amount administered is in the range of from about 13 micrograms up to about 1000 micrograms.

10. The method of causing the reduction of physiological and/or subjective reactivity to stress in a human being subjected to stress which comprises administering to said human transdermally or through inhalation an eff ctive

amount of a composition of matter consisting essentially of:

(a) a stress reactivity-reducing substance selected from the group consisting of:

Nutmeg Oil;

Mace Extract;

Neroli Oil; and

Valerian Oil;

(b) a carrier perfume composition compatible with said stress reactivity reducing substances;

and (c) ethanol

the weight ratio of said stress reactivity reducing substance to said carrier perfume composition being in the range of from about 1:100 up to about 100:1 and the weight ratio of said stress reactivity-reducing substance to said ethanol being in the range of from about 1:99 up to about 99:1.

11. The method of claim 12, wherein the stress reactivity reducing substance is nutmeg oil and the amount administered is in the range of from about 13 micrograms up to about 1000 micrograms.

12. The method of causing the reduction of physiological and/or subjective reactivity to stress in a human subjected to stress which comprises administering to said human transdermally or through inhalation an effective amount of a stress reactivity-reducing substance selected from the group consisting of:

Myristicin;

Elemicin; and

Isoelemicin.

13. The method of claim 9, wherein the stress reactivity-reducing substance is myristicin and the myristicin is administered in an amount of from about 0.013 micrograms up to about 50 micrograms.

14. The method of causing the reduction of physiological and/or subjective reactivity to stress in a human subjected to stress which comprises administering to said human transdermally or through inhalation an effective amount of

a composition of matter consisting essentially of:

(a) a str ss reactivity-reducing substanc selected from the group consisting of:

Myristicin;

Elemicin; and

Isoelemicin;

and (b) a carrier perfume composition compatible with said stress reactivity-reducing substance

the weight ratio of said stress reactivity-reducing substance to said carrier perfume composition being in the range of from about 1:100 up to about 100:1.

15. The method of claim 14, wherein the stress reactivity-reducing substance is myristicin and the myristicin is administered in an amount of from about 0.013 micrograms up to about 50 micrograms.

16. The method of causing the reduction of physiological and/or subjective reactivity to stress in a human subjected to stress which comprises administering to said human transdermally or through inhalation an effective amount of a composition of matter consisting essentially of:

(a) a stress reactivity-reducing substance selected from the group consisting of:

Myristicin;

Elemicin; and

Isoelemicin;

and (b) ethyl alcohol;

the weight ratio of said stress reactivity-reducing substance to said ethyl alcohol being in the range of from about 1:99 up to about 99:1.

17. The process of claim 16, wherein the stress reactivity-reducing substance is myristicin and the myristicin is administered in an amount of from about 0.013 micrograms up to about 50 micrograms.

18. A method for detecting physiological and/or subjective reactivity to stress in a human comprising testing a human likely to exhibit physiological and/or subjectiv reactivity by:

(i) measuring the initial blood pressure and mood of said human; then

(ii) applying stress to said human; then

(iii) simultaneously therewith measuring blood pressure and mood changes resulting from the application of said stress to said human; thereafter

(iv) administering to said human a substance which is to be tested as being effective to cause the reduction of physiological and/or subjective reactivity to said stress; and

(v) measuring blood pressure and mood changes resulting from the administering to said human of said substance which is to be tested as being effective in causing the reduction of physiological and/or subjective reactivity to stress.

19. The method of claim 18, wherein the stress reactivity-reducing substance to be tested is selected from the group consisting of:

Nutmeg Oil;
Mace Extract;
Neroli Oil;
Valerian Oil;
Myristicin;
Elemicin; and
Isoelemicin.

20. The method of causing the reduction of physiological and/or subjective reactivity to stress in a human subjected to stress which comprises exposing said human transdermally or through inhalation to an effective stress reactivity-reducing amount of a composition of matter consisting essentially of an effective stress reactivity reducing substance selected from the group consisting of:

Nutmeg Oil;
Mace Extract;
Neroli Oil; and
Valerian Oil

in intimate admixture with a carrier perfumed article compatible with said stress reactivity reducing substance.

21. The method of claim 17, wherein the stress reactivity reducing substance is nutmeg oil and the nutmeg oil is present in the carrier perfumed article in an amount to cause said human to be treated with said nutmeg oil in an amount of from about 13 micrograms up to about 1000 micrograms of nutmeg oil.

22. The method of causing the reduction of physiological and/or subjective reactivity to stress in a human subjected to stress which comprises exposing said human transdermally or through inhalation to an effective stress reactivity-reducing amount of a composition of matter consisting essentially of an effective stress reactivity-reducing substance selected from the group consisting of:

Myristicin;

Elemicin; and

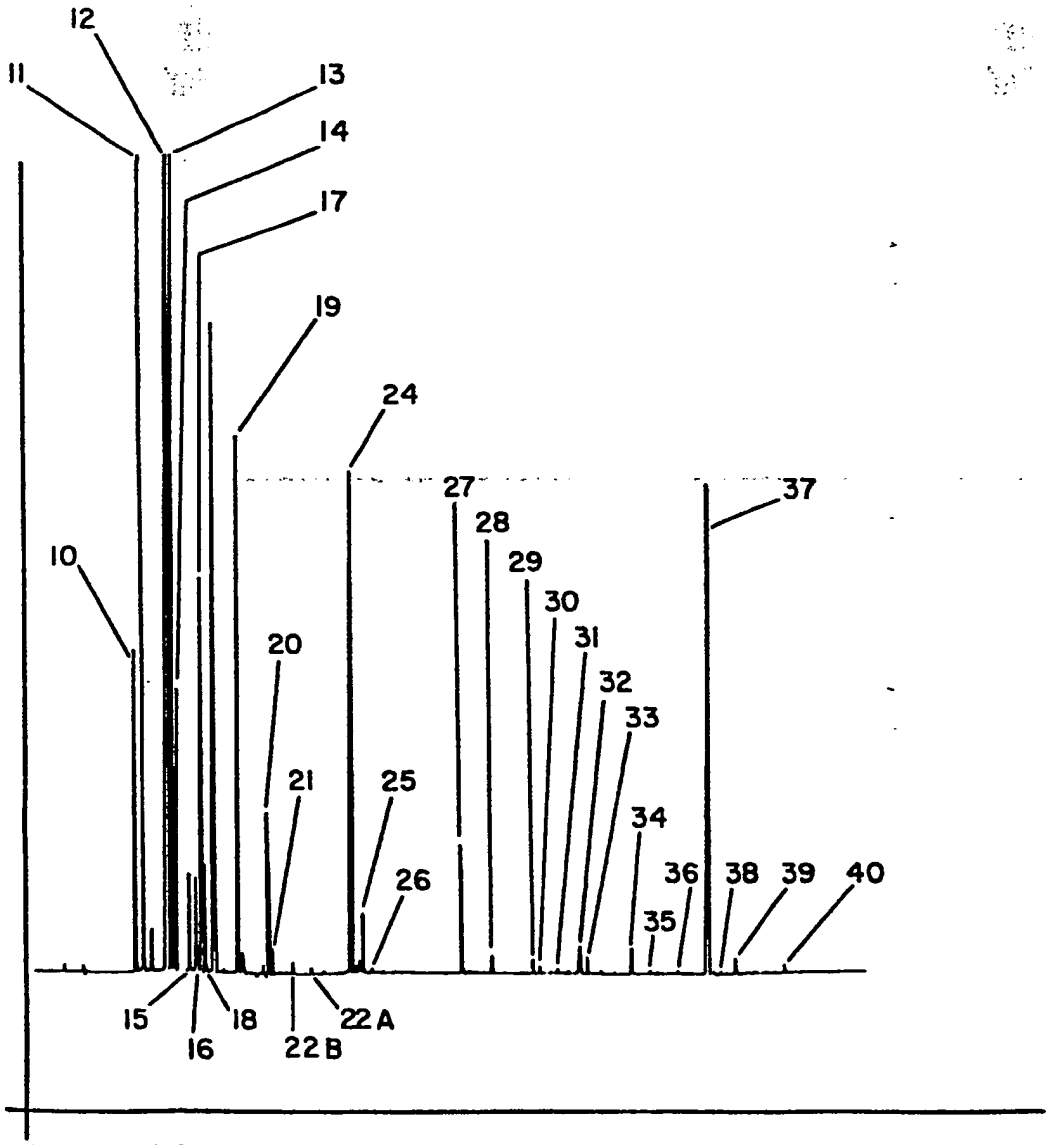
Isoelemicin

in intimate contact with a carrier perfumed article compatible with said stress reactivity reducing substance.

23. The method of claim 22, wherein the stress reactivity reducing substance is myristicin and the myristicin is present in the carrier perfumed article in an amount to cause said human to be treated with said myristicin in an amount of from about 0.013 micrograms up to about 50 micrograms of myristicin.

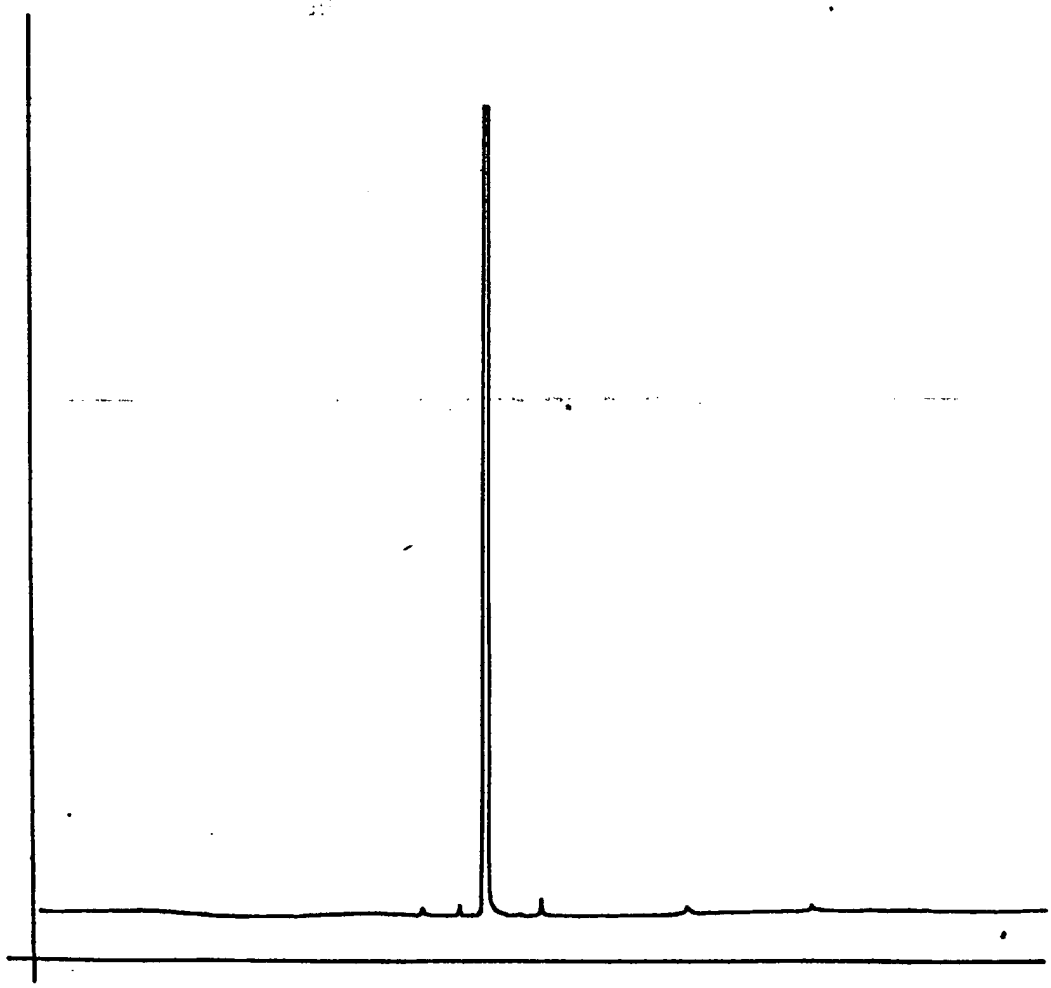
24. Toothpaste comprising one or more of nutmeg oil, mace extract, neroli oil, valerian oil, myristicin, elemicin and isoelemicin.

FIG.1



GLC PROFILE FOR EXAMPLE I.

FIG.2



GLC PROFILE FOR BULKED FRACTIONS 7-12 OF EXAMPLE I.

FIG. 3
EXAMPLE III

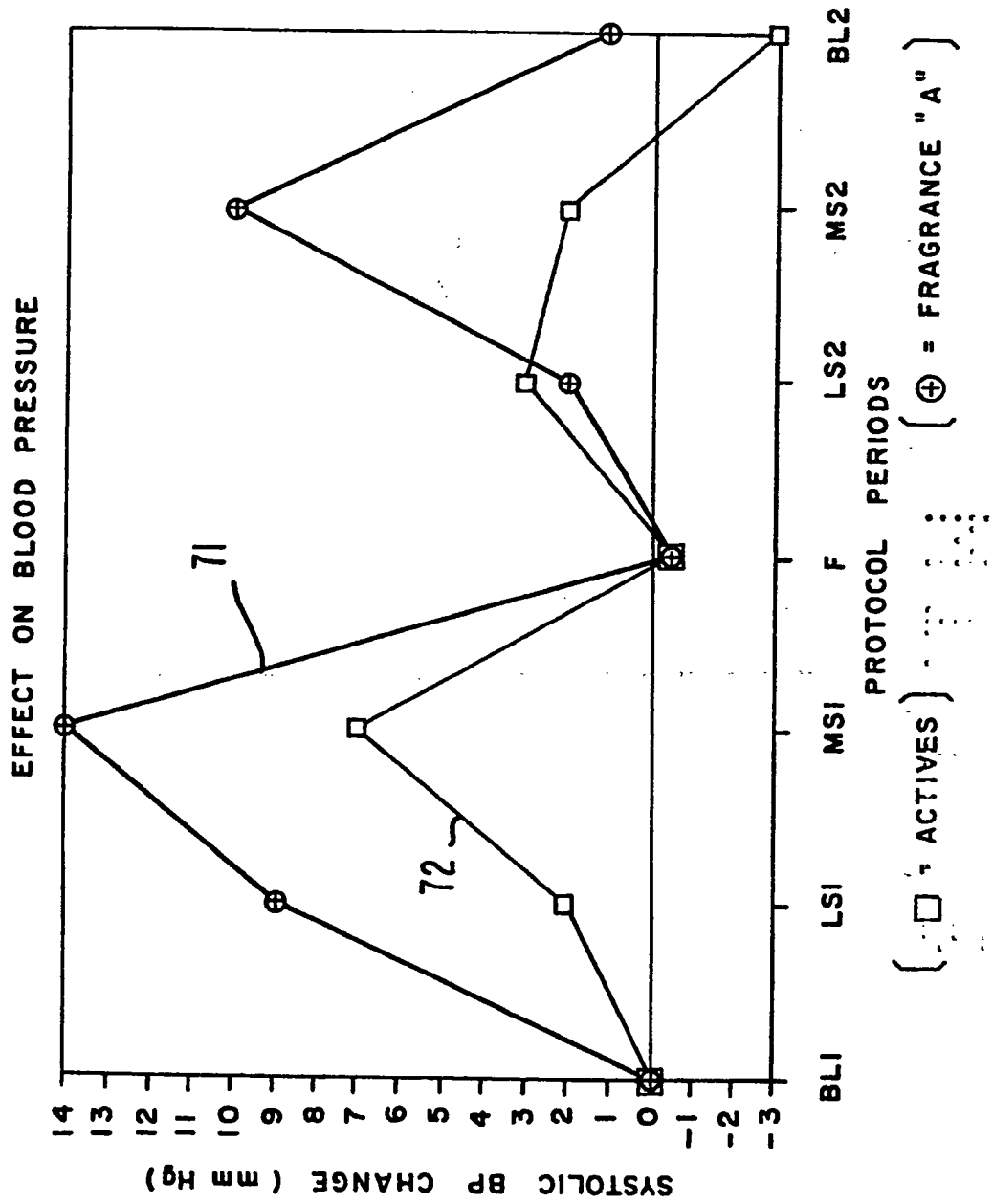


FIG.4
EXAMPLE IV.

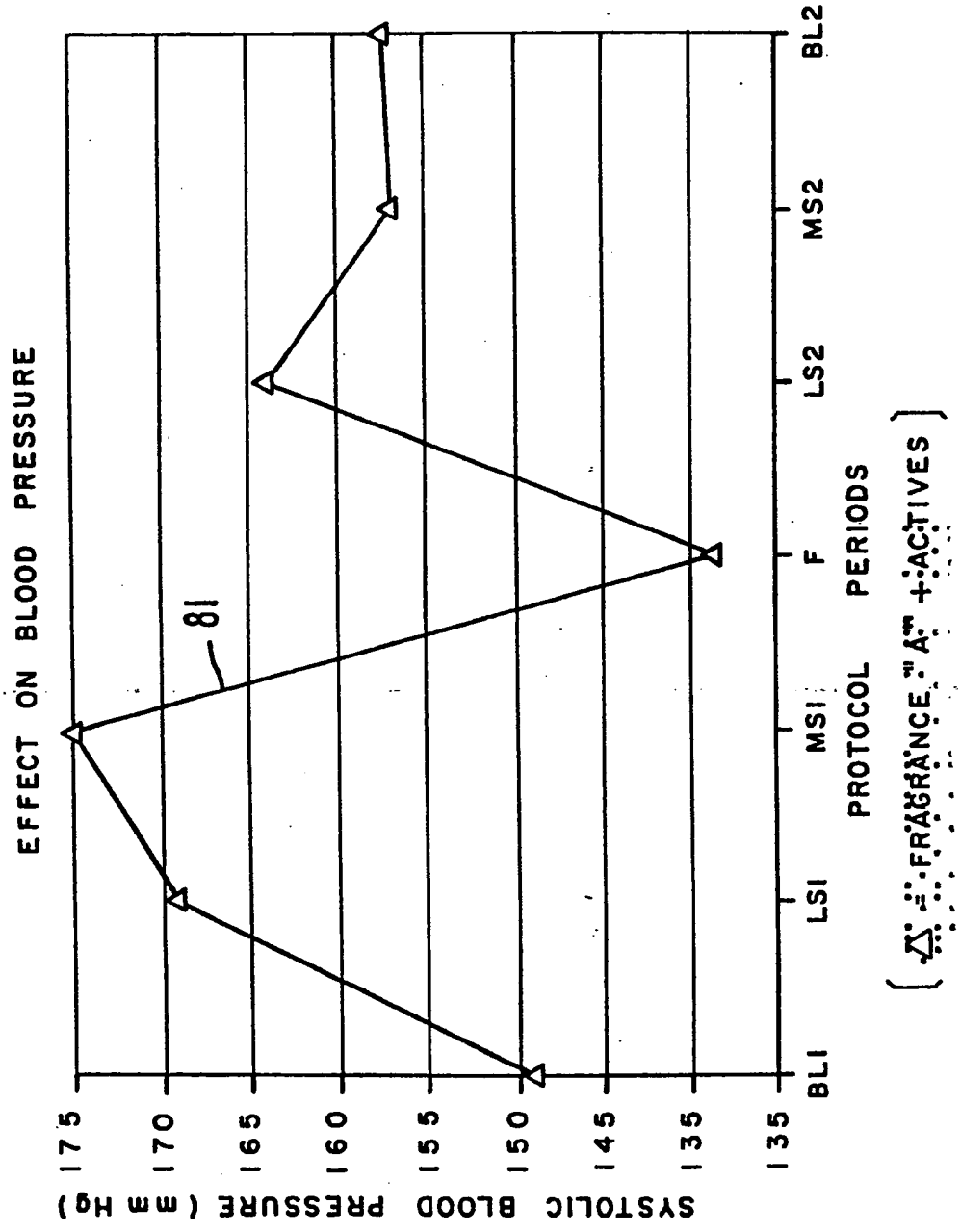
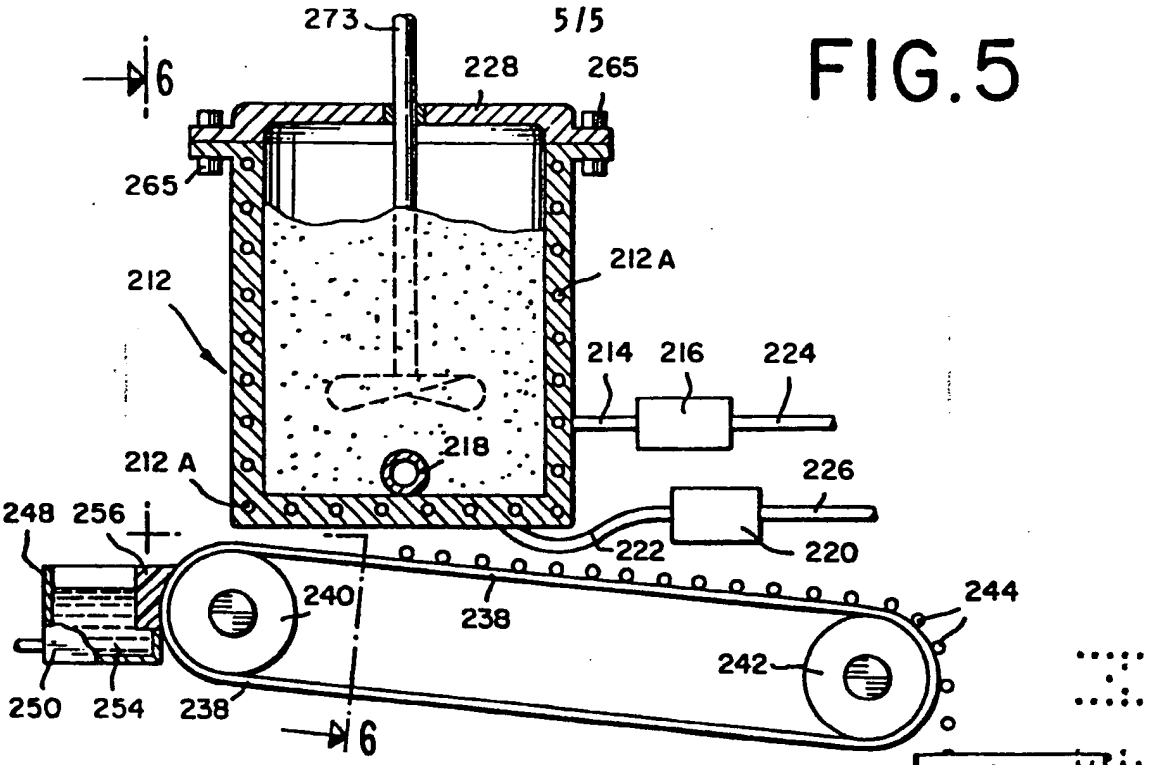


FIG.5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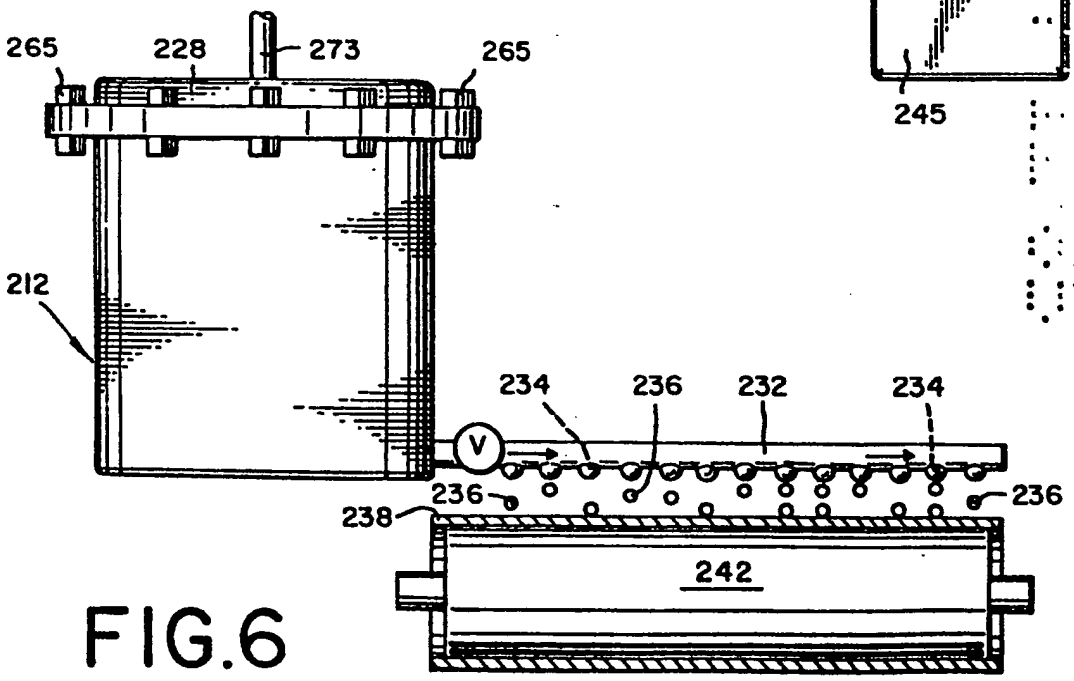
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FIG.6